Issue on Tumors of the Chest

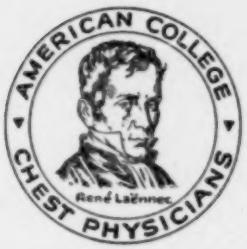
VOLUME XVII NUMBER 6

DISEASES

of the

CHEST

OFFICIAL PUBLICATION



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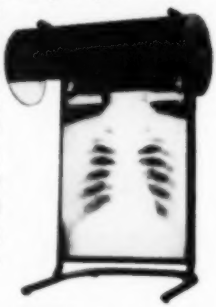

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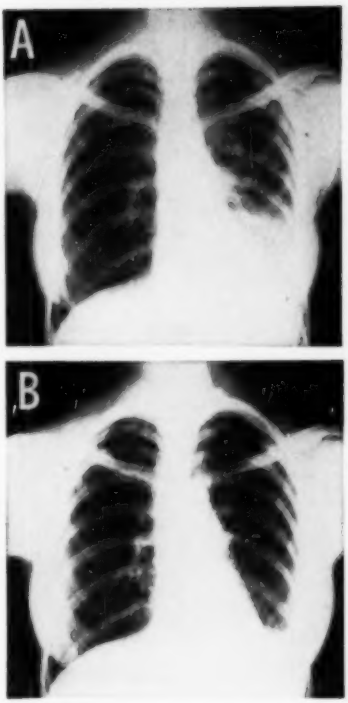

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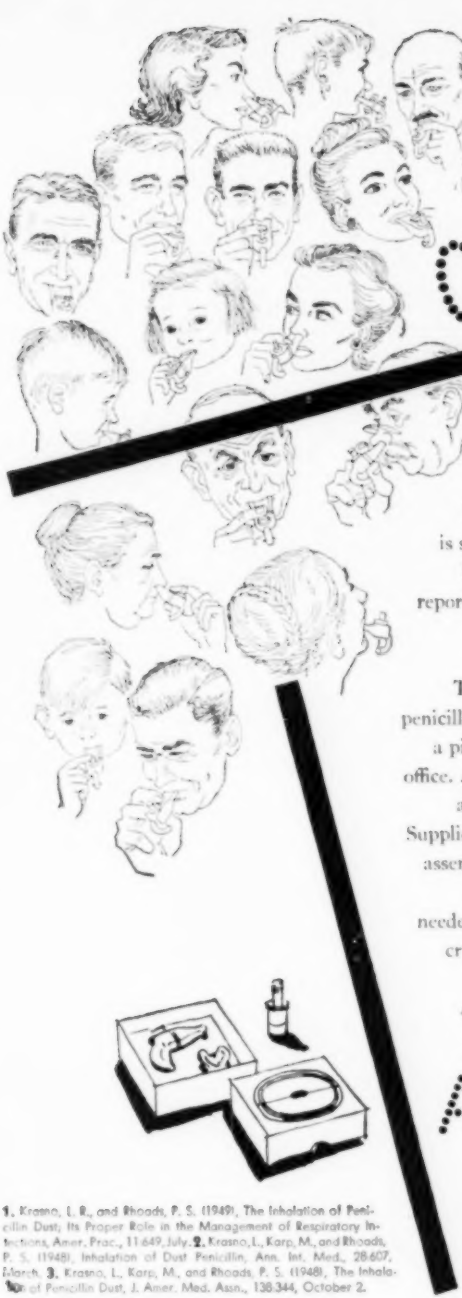

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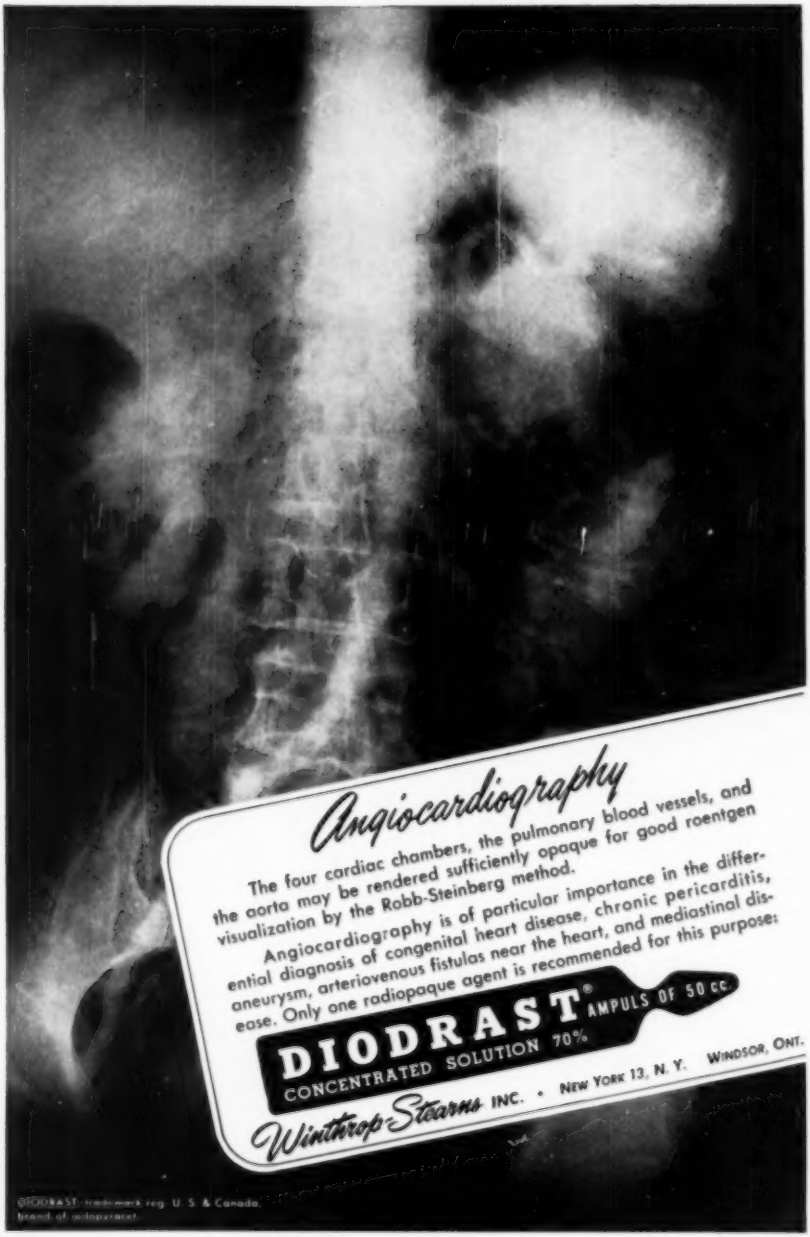
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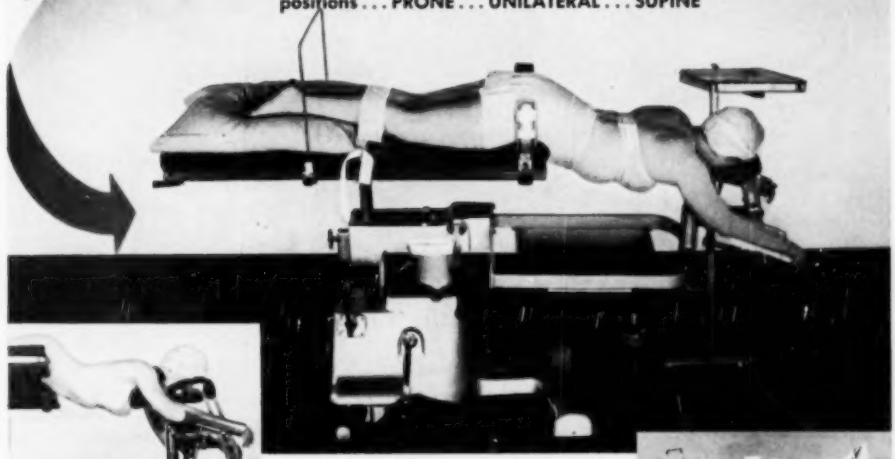

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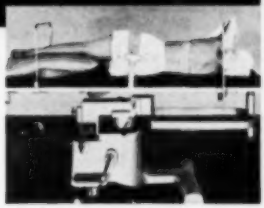

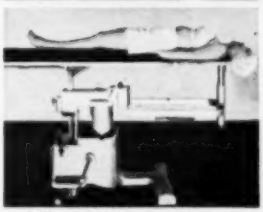

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DISEASES *of the* CHEST

VOL. XVII JUNE 1950 NUMBER 6

Introduction

Modern diagnostic methods offer an ever increasing proficiency in the diagnosis of chest diseases. This is especially true with reference to tumors of the chest. The reliability of cytological diagnosis of cancer of the lung, which is rapidly gaining acceptance and wide clinical application, is a good example in point. Various roentgenologic procedures, such as tomography, angiocardiography, kymography, positional x-ray photography, bronchography and the use of esophageal contrast medium are adding substantially to the successful diagnostic exploration of the chest. Also, procedures, such as bronchoscopy, esophagoscopy, thoracoscopy, the use of radioactive isotopes, endocrinologic assaying of the blood, artificial pneumothorax and pneumoperitoneum, exploratory thoracotomy and others contribute in no small manner to competent differential diagnosis of neoplastic conditions of the chest.

Trivial though it may sound, it is axiomatic that the earlier thoracic tumors are discovered the better the chances for effective therapeutic intervention. Certainly, the unprecedented achievements attained by thoracic surgery in recent years were not anticipated by the most imaginative surgeons of a quarter of a century ago. Undoubtedly, with further progress in diagnosis, anesthesia, surgical technique and with the application of standard biophysical principles, attention to nutritional requirements, adequate preoperative and postoperative measures and the use of antibiotics, recovery and life expectancy in patients with tumors of the chest will be even more favorably affected than heretofore. The optimism in this respect is supported by satisfactory records relative to the therapeutic application of x-ray irradiation, radium, radioactive isotopes, nitrogen mustards and endocrine substances in the management of certain well selected cases of thoracic newgrowths.

This issue of *Diseases of the Chest* is devoted to the collective presentation of recent advances in the diagnosis and treatment of primary and metastatic, benign and malignant tumors of the chest. It is hoped that with this symposium, a worthwhile and timely contribution has been made to the welfare of those who are in need of the services of the medical profession in general and the chest specialist in particular.

Andrew L. Banyai, M.D., F.A.C.P., F.C.C.P.

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Primary Neoplasms of the Lung*

DUANE CARR, M.D., F.C.C.P., EDWARD F. SKINNER, M.D.,
S. GWIN ROBBINS, M.D. and CHARLES R. KESSLER, M.D.
Memphis, Tennessee

The amazing variety of primary neoplasms of the lung and the frequency with which they are encountered is appreciated more widely now than at any other period in the history of medicine. They were once thought by clinicians to be rare pathological curiosities, their antemortem diagnosis next to impossible, and treatment of them so unsatisfactory as to make a careful search for them a waste of time and effort.

Now that extirpation of these tumors has become a relatively safe practice, and thoracic surgery is generally available in most sections of the country, there is more reason for all physicians to be interested in their detection and early recognition. This fact, with the ever increasing use of community-wide mass x-ray surveys, has caused the discovery of more and more of these potentially fatal neoplasms at a stage in which a cure is possible. It has also disclosed that many of the chronic or persistent infectious diseases of the lungs are due to bronchial occlusion by tumors which are amenable only to corrective surgery.

The following pages contain an outline of the various types of primary neoplasms to be found in the lungs, a description of the means of their detection, and a discussion of the possibilities for their treatment.

Pathology

All of the several primary pulmonary neoplasms, with the probable exception of alveolar cell carcinoma, have their origin in the bronchial tissues. They vary in malignancy from those which are apparently benign to some which are classified as Grade II according to their cellular characteristics. However, almost all of the so-called benign growths have been reported to undergo malignant changes at one time or another, so that one finds it difficult to be reassured in regard to any intrapulmonary tumor's harmlessness because of its behavior or apparent benignancy.

The following is a list of the pathologic types of primary neoplasm in the lung found in the records of our own hospitals (John Gaston Hospital and Baptist Memorial Hospital), and gleaned from the literature:

*From the Department of Surgery, University of Tennessee College of Medicine.

1. Bronchiogenic Carcinoma.
2. Bronchial Adenoma and Cylindroma ("Mixed Tumors").
3. Hamartoma and Chondroma.
4. Lipoma.
5. Fibroma.
6. Hemangioma.
7. Myoblastoma.
8. Sarcoma and Fibrosarcoma.
9. Alveolar Cell Carcinoma.
10. Superior sulcus (Pancoast's) tumor.

Tuberculoma is not a true neoplasm, though it must be considered in any differential diagnosis of a mass lying within the lung, and will not receive detailed consideration as a primary neoplasm.

Bronchiogenic Carcinoma

Bronchiogenic carcinoma has been classified by Jaffe into four types according to the site of origin: 1) the central or hilar type which has its origin in a main bronchus, 2) the intermediary type originating in a bronchus of the third, fourth or fifth order, 3) the peripheral type which has its beginning in a bronchus near the pleura, and 4) the diffuse type.

Microscopically, these tumors possess a large degree of pleomorphism. However, certain cell types do predominate, and this has lead to a more widely used classification by Fried based upon the cellular composition of the tumor.

1. Squamous cell carcinoma:
   a) keratinizing,
   b) non-keratinizing,
   c) oat cell,
   d) anaplastic.
2. Adenocarcinoma:
   a) simple,
   b) papillary,
   c) mucocellular.
3. Round Cell Carcinoma.

Other pathologists include round cell carcinoma and anaplastic squamous cell carcinoma in the classification of undifferentiated carcinoma.

Though the frequency of each type varies somewhat in the published series in the literature, approximately 75 per cent of bronchial carcinomas are of the squamous cell type, 12 per cent adenocarcinoma and other types 13 per cent according to Fried. In our series and in the Memorial Hospital series, squamous cell

carcinoma comprises approximately 40 per cent, adenocarcinoma 20 per cent and undifferentiated carcinoma 40 per cent.

The gross appearance of a bronchial carcinoma is that of an opaque, yellowish-white, firm and irregular mass invading the lung in broad sheets. Occasionally, however, the mass appears to be encapsulated, rounded, and sharply demarcated from the surrounding tissues, giving the gross appearance of a benign tumor. In the course of the advance of the carcinoma in the lung there is produced a fibrous tissue stroma, especially in squamous cell carcinoma, which holds the carcinoma cells together with distinct intercellular bridges (prickle cells).

Study of resected specimens reveals that the carcinoma tends to extend along the adjacent submucosal tissue of the bronchus for considerable distances beyond the limits of visible or palpable tumor; as much as 2 cm. in the case of adenocarcinoma and 1.5 cm. in squamous cell carcinoma.

In an estimated 15 per cent of cases of carcinoma of the bronchus the tumor outgrows its blood supply and with the help of aerobic and anaerobic organisms develops central necrosis. The detritus may be evacuated through a bronchus and produce a large cavity which frequently contains a fluid level upon x-ray examination, and closely resembles ordinary pyogenic lung abscess.

Changes may take place in pulmonary tissue which is not actually invaded by tumor. Partial bronchial occlusion results in an obstructive emphysema that frequently produces bullae which may reach large proportions and which may rupture, resulting in spontaneous pneumothorax. More often, atelectasis of a lobe or an entire lung develops, complicated by pneumonitis and obliterating bronchiolitis with resulting bronchiectasis and lung abscess.

Metastases by the lymphatic and hematogenous routes are most common, and a bronchial carcinoma may also spread by direct extension into contiguous structures. Ochsner and DeBakey analyzed 2,579 collected cases and found metastases to the regional lymph nodes in 75.9 per cent; liver 34.4 per cent; bones 24.4 per cent; adrenal glands 17.6 per cent; kidneys 16 per cent; brain 14.6 per cent; heart and pericardium 10 per cent; and pancreas 5.1 per cent.

In 100 cases Jaffe found regional lymph node metastases in all but two patients.

Pleural effusions, frequently sero-sanguinous, are commonly found late in the course of the disease. The value of cell blocks prepared from centrifuged pleural exudate should be stressed. In as high as 94 per cent of cases in which carcinoma of the lung is present and complicated by effusion positive evidence of carcinoma cells in the pleural fluid will be found.

Mixed Tumors of the Lung

There is a group of bronchial tumors which was once thought to be benign and which is characterized by slow growth, and has a cellular structure which for long periods of time lacks the indications of malignancy. These tumors protrude into the lumen of the bronchus, usually present a smoothly rounded surface covered with normal appearing epithelium, and surface erosion is rare. Microscopically, the bronchial epithelium often is shown to have undergone squamous metaplasia and beneath this is a layer of fibrous tissue of varying thickness within which lies the main portion of the tumor. The predominating cells are usually small round cells with scanty cytoplasm and darkly staining nuclei in which mitotic division is rarely seen. The resemblance to fetal pulmonary alveoli is very striking, and the majority of these tumors were once loosely classified as bronchial adenomata.

However, the stroma in some cases is dominated by cells of mesoblastic origin including smooth muscle, hyaline cartilage, fat and sometimes even bone. This fact lead Graham and Womack to designate these tumors in 1938 as "mixed tumors of the lung."

Much credit belongs to Graham and Womack for clarifying both the histology and the histogenesis of these mixed tumors of the bronchus. In accordance with their views, two groups of tumors arise as a result of the failure of the bronchial bud to develop into the normal arrangement of adult tissues. The first group contains those "in which mesodermal elements predominate." The second group is that in which "the entodermal or epithelial elements are dominant." The former group includes such tumors as chondroma, osteoma, lipoma, fibroma, angioma, myxoma and (in their malignant phase) sarcoma. The second group consists chiefly of adenomas and cylindromas.

Just what proportion of these tumors undergoes malignant change is not known at present. Graham and Womack, Anderson, Chamberlain, Goldman, and others have reported such cases that emphasize the potential malignant qualities of these neoplasms. There is general agreement that most surgically removed specimens reveal only local invasion of pulmonary tissue and occasional regional lymph node involvement. The five-year survival rate of patients from whom such tumors showing local invasion have been removed is between 80 and 90 per cent, indicating that their malignancy is relatively slight when compared with that of bronchiogenic carcinoma. It is felt that observation for several decades will be necessary before the final survival rate following their resection will be known.

Goldman recently reported two cases of the mixed tumor type

which ended in death. Endoscopic removal and irradiation therapy was followed later by recurrence of the tumor, in one case at the bifurcation of the trachea. He states that after a period of six years of observation and treatment "there is no doubt that a mixed tumor type of adenoma had become a highly malignant carcinoma, nor is there any doubt that if this neoplasm were seen only at postmortem and without the biopsy six years earlier, it would have been diagnosed as an undifferentiated bronchiogenic carcinoma."

Bronchial adenoma and cylindroma are presented in another paper in this issue.

Hamartoma and Chondroma

Hamartoma and chondroma of the lung belong to a group of tumors of the bronchus which are relatively benign. Histologically, these tumors consist of normal epithelial and mesodermal bronchial tissue cells which in their development have become distorted in their pattern, resulting in an abnormal mixing and arrangement of these tissues. Many of these tumors have been called chondromas because of the predominance of cartilage, but other tissue elements are present and thus they are not pure chondromas. The term "hamartoma" is more generally used.

Grossly these tumors are white or light gray and are sharply demarcated from the surrounding lung. The cut surface appears lobulated and calcium is frequently scattered throughout the tumor. Its size varies from that of a black-eyed pea to one that fills the entire hemithorax. In 26 of 30 cases Hickey and Simpson found that the tumor was subpleural; in the remaining four cases it was near the hilum of the lung. In the vast majority of cases the extension of the tumor is extrabronchial, although a few cases have been reported in which polypoid endobronchial hamartomas consisted of epithelium, fat, smooth muscle, cartilage and bone, with cartilage the predominant element in most cases. Multiple islands of cartilage surrounded by perichondrium are frequently found and portions of this cartilage have often undergone calcification. Fat is found scattered in these tumors in approximately one-half of the reported cases. Epithelial elements are frequently present, often giving rise to mucous cysts. In some cases the epithelial lining of these cysts is ciliated. Malignant changes in these tumors rarely occur.

Lipoma, Fibroma, Hemangioma and Myoblastoma

Lipoma, fibroma, hemangioma and myoblastoma may be classified as variants of the mixed type of bronchial tumor in which a specific type of cell of mesothelial origin predominates.

The lipomas are often pedunculated, smooth, round and covered

with normal mucous membrane. Microscopically, the lesion consists of lobules of mature fat cells with a delicate fibrous tissue stroma. In the case described by Watts, no muscle, cartilage or bone was present. Mature fat cells do appear in varying proportions in others of the so-called benign tumor groups in which different cellular types are dominant. The lipomas apparently arise from adipose tissue normally present in the bronchial walls.

Although all reported lipomas are histologically benign, because of bronchial occlusion serious and even fatal suppuration distal to them may occur.

Fibromas were found by Lindgren to represent about 9 per cent of the so-called benign bronchial tumors in his review of this subject, but many of them showed varying proportions of fat, muscle and angiomatous tissue indicating their close relation to the mixed tumor group. Instances of malignant change were found.

Hamangiomas of the bronchus have been reported occasionally, and one in our experience was a smoothly rounded tumor projecting into the lumen of the right lower lobe bronchus covered by normal mucous membrane. Blood channels were large and diffusely irregular with a light fibrous tissue stroma surrounding them. No evidence of malignant change was observed.

Kramer in 1939 reported a pedunculated and apparently benign tumor in the right lower lobe bronchus which he characterized as a myoblastoma.

Sarcoma and Fibrosarcoma

Sarcoma and fibrosarcoma of the lung are extremely rare and appear most frequently in children and young adults. Many of the reported cases have proved upon review to be undifferentiated or anaplastic bronchiogenic carcinoma. In our own hospitals three such sarcoma cases were found in the past ten years, and review of the tissue specimens by Dr. Douglas Sprunt* resulted in their re-classification as anaplastic carcinoma.

Stout has done much to clarify this subject. He accepts as true fibrosarcomas only those tumors composed of fibroblasts which produce collagen and reticulum fibers, the latter being wrapped around the cells in a characteristic fashion. Collagen may be absent in the more undifferentiated fibrosarcomas. By eliminating all cases which did not fulfill his criteria, Stout could accept only six cases previously published in the literature as being true fibrosarcomas.

Womack and Graham cite the extremely interesting case of a pneumonectomy performed for an invasive tumor of the right

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upper lobe. Upon microscopic examination the epithelial and connective tissue had both become malignant. The epithelial elements were extremely anaplastic, rapidly growing, and with numerous mitotic figures. "The stroma was extremely cellular, with spindle-shaped cells whose nuclei showed evidence of rapid growth with numerous mitotic figures." This is an outstanding example of a tumor that Graham believes would have been called an adenoma had it been seen early, before its malignant transformation. They designate this tumor as a "carcinoma-sarcoma."

Alveolar Cell Carcinoma

Alveolar cell carcinoma has attracted a great deal of interest recently because the preponderance of evidence makes us classify this malignant pulmonary neoplasm as multicentric in origin. It is also known as pulmonary adenomatosis and is histologically similar to the virus disease of sheep known as jagziekte disease. These facts lead to an interesting bit of speculation in regard to the possible role of virus infections in the production of carcinoma.

The fundamental feature of alveolar cell carcinoma is the definite reproduction of alveolar structure. The malignant cells lining the alveoli are dark-staining, tend to be polygonal and have abundant eosinophilic cytoplasm. The cells are frequently in multiple layers, and the alveoli are often filled with these obviously malignant cells which show frequent mitoses. Malignant areas are separated grossly and microscopically by normal parenchyma, with masses and cords of wildly growing cells in a fibrous tissue stroma in the more malignant cases. A single lobe may be involved, or all lobes may be involved simultaneously with a diffuse distribution of discrete nodules which become coalescent as the growth progresses.

Metastases occur by way of the lymphatic channels to the regional lymph nodes and occasional distant metastases have occurred.

The Superior Sulcus Tumor (Pancoast's Tumor)

The superior sulcus tumor (Pancoast's tumor) is not a pathologic entity in itself but is the syndrome of a tumor which involves the cervical sympathetic chain and brachial plexus, and produces local bone destruction. In five of Pancoast's original cases no pathological diagnosis was made, but his description of the others was compatible with the various types of bronchiogenic carcinoma. Other types of neoplasm, however, have produced the same syndrome, such as the sympathoblastoma and carcinoma of the thymus. In our experience, and in that of others, neurofibromas have likewise fulfilled the criteria of a so-called Pancoast tumor.

Diagnosis

The *index of suspicion* on the part of the patient's physician is the most important single factor in the diagnosis of any primary lung tumor. These tumors occur frequently enough so that almost any busy practitioner will see two or three annually. Some of them are "silent" and are discovered only upon routine x-ray films made upon apparently healthy people, but there are certain cardinal symptoms which will arouse suspicion in the minds of alert practitioners in a large number of cases.

Cough, although a symptom common to many disorders of the respiratory tract, becomes significant when it changes in character. *Pain*, or a sensation of discomfort, in the chest is commonly experienced. *Dyspnea* on exertion is present as atelectasis develops or pleural fluid forms. *Wheezing*, remarkably similar to asthma and often relieved by adrenin, results from partial bronchial occlusion and disappears as total occlusion ensues. *Hemoptysis*, particularly blood streaked sputum, is a valuable suspicion-arouser. *Hoarseness*, or weakening voice, in the absence of an intrinsic laryngeal lesion indicates invasion of, or pressure upon, the recurrent laryngeal nerve. *Rheumatism*, a form of pulmonary osteoarthropathy, frequently is associated with pulmonary neoplasm. And finally, *persistent* or *recurring pulmonary infection*, frequently vulgarly called *"virus pneumonia,"* should ring a bell to awaken any suspicion not previously aroused.

In our experience the advent of an increasing array of antibiotics is anything but an advantage to the patient with a primary neoplasm of the lungs. It takes longer now for a physician to systematically give each agent a thorough trial, and the temporary benefit experienced by the patient as his infection is subdued may allay suspicion of a tumor for surprising periods of time (Case 1).

Once a tumor of the lung is suspected, an orderly examination is indicated and the suggested outline is designed to reveal the diagnosis as early as possible in the series of examinations and with the minimum of expense to the patient:

1. Complete physical examination.
2. Fluoroscopy.
3. Laboratory,
   Blood counts and differential smear,
   Blood sedimentation rate,
   Sputum for tumor cells, tuberculosis, or fungus.
4. X-ray films of the chest,
   Postero-anterior and lateral projections,
   Diagonals (if needed).

5. Bronchoscopy,
   Biopsy,
   Bronchial lavage for cellular studies.
6. Bronchograms.
7. Laminagrams (or Bucky grid films).
8. Angiograms.
9. Surgical exploration (or biopsy of peripheral nodes).

Carcinoma of the bronchus is the most frequently encountered primary tumor of the lungs and is therefore the first to be suspected and sought out. Fortunately, most of the other primary neoplasms will be revealed in the course of an attempt to prove or disprove the presence of a carcinoma.

Diagnosis of a *bronchiogenic carcinoma* is often rendered difficult because of the associated pulmonary infection produced by interference with bronchial drainage. The clinical and x-ray pattern may be indistinguishable from tuberculosis (Case 2), even to cavity formation. Interstitial pneumonitis and abscesses often complicate the picture, and the diffuse infiltrating type of carcinoma closely resembles fungus infections in its clinical and roentgenologic manifestations. To further complicate the diagnosis, non-pathogenic Monilia are often found in the sputum, as are acid-fast forms of saprophytic actinomycetes.

The physical examination will often fail to reveal direct signs of a tumor in the chest, but indirect evidence can frequently be detected in the form of wheezing, or from signs of atelectasis, pneumonitis, suppuration or pleural fluid. A complete history and physical examination, meticulously carried out, is of importance to detect primary tumors elsewhere in the body to which the lung neoplasm may be secondary, and to reveal evidence of extension or metastases from a primary lung neoplasm outside of the lung itself.

The physical examination should include a particularly careful search for *enlarged lymph nodes* in the supraclavicular fossae, axillae and abdomen. In fact, the entire body should be palpated for nodules. A recent patient of ours was spared an exploratory operation by the discovery of a small pea-sized subcutaneous metastatic node on the anterior chest wall. In the *eyes* one may find a contracted pupil or a ptosis of the lid, part of a Horner's syndrome indicating involvement of the lower cervical sympathetic ganglia. The *larynx* may show impaired motion of one vocal cord which indicates invasion of, or pressure upon, one recurrent laryngeal nerve, even before marked changes in the voice take place. The *genitals* and *prostate* deserve attention because the former may be the site of origin of a single metastatic tumor in the lungs

which otherwise resembles a primary growth (solitary metastasis of a seminoma, for instance), and the latter occasionally gives rise to diffuse metastatic carcinoma in the lungs. The *extremities* must be inspected and palpated for evidence of pulmonary osteoarthropathy (clubbing, etc.) and for primary tumors of bone which may produce solitary pulmonary metastases resembling primary neoplasms.

Fluoroscopy of the chest is valuable to show evidence of obstructive emphysema, a "lighting up" of a segment or lobe on expiration, when a bronchus is partially occluded by any of the primary tumors. It also is the only means of detecting paralysis of one side of the diaphragm when it exhibits paradoxical motion as the patient inhales sharply, which would indicate involvement of the phrenic nerve. Pleural fluid is readily detected and located for aspiration by means of the fluoroscope.

The total blood counts and differential white cell count are apparently unaffected directly by a primary neoplasm of the lungs, and changes are more often due to associated pulmonary infection present. *Anemia*, when present, is usually of the secondary or hypochromic variety in contrast to that found in carcinoma of the stomach. The *blood sedimentation rate* is usually elevated in the presence of malignant lung tumors and serves only to arouse suspicion of their presence, or to help confirm one's impression of their malignancy. Insufficient data are available as yet to establish the place of *serological tests* for malignancy in the diagnosis of pulmonary neoplasms, especially since tuberculosis frequently produces a false positive result.

Sputum examination for cancer is gaining in popularity as experience with the method is acquired in various medical centers and hospitals. Expectorated specimens may be smeared while fresh and examined by the technic of Papanicolaou, or bronchial washings may be obtained, centrifuged and imbedded for staining with hemotoxylin and eosin. The bronchial lavage can easily be performed as an office procedure using ten cubic centimeters of a normal saline solution in the same manner as iodized oil is instilled for bronchograms, as described by Carr et al. Wandall identified bronchiogenic carcinoma from sputum examinations in 84 of 100 patients, and others are reporting similar results.

The standard x-ray examination of the chest, while one of our most valuable aids in the detection of primary lung tumors, often fails to reveal the shadow of the tumor itself. Lateral views and often diagonal projections will show shadows behind the heart shadow or diaphragm which are not to be seen on the conventional film. Even then the evidence provided by the x-ray films may

only indirectly point to the presence of a tumor; atelectasis of a lobe or lobule, interstitial pneumonitis, an abscess, "virus pneumonia," apparent tuberculosis or pleural fluid.

Certainly absence of a tumor shadow is insufficient evidence upon which to *rule out* the existence of a lung tumor when symptoms or signs indicate the possibility of its presence. All too often an early carcinoma or other bronchial neoplasm casts no recognizable shadow on the x-ray film or is concealed by shadows of other structures.

When definite tumor shadows are seen on the x-ray films, it is impossible to identify with certainty the type of neoplasm which casts them. Bronchial carcinoma, as well as the less malignant tumors, may appear to be a discrete, sharply circumscribed intrapulmonary tumor which grows at an imperceptible rate and has the appearance of a benign tumor. Yet more of these circumscribed shadows are due to carcinoma, and malignant, than are due to adenomas, hamartomas and all the rest of the less malignant mixed tumors combined.

Bronchography is of value in demonstrating the presence of neoplasms in the bronchi, especially when they lie in the smaller bronchi beyond the visible range of bronchoscopy. A persistent filling defect on repeated examinations must be viewed as strong evidence in favor of a primary lung tumor.

Bucky grid films, laminagrams and angiograms are each useful under certain conditions to help delineate tumors from surrounding atelectasis or areas of infection, and to differentiate neoplasms from vascular anomalies or diseases.

Bronchoscopic examination of the patient suspected of having a primary neoplasm of the lung is absolutely indicated. A high proportion of lung tumors can be detected directly or indirectly by this means, and it is also necessary to help determine the probable operability of the patient's lesion.

About 40 per cent of all bronchial tumors originate within the visible portions of the bronchial tree where they can be seen directly through a standard type bronchoscope and a biopsy of them taken. Right angle and retrograde-viewing bronchoscopes, though not yet universally used, are improving this figure. Herbut and Clerf report positive biopsies obtained from 71 of 180 patients who had proved bronchiogenic carcinoma, or 39 per cent. Even a higher rate of positive diagnosis was obtained by them by examination of bronchial secretions in which they found cancer cells in 161 of the 180, or 89 per cent.

It must be emphasized that a single negative biopsy is insufficient to exclude the presence of a bronchial neoplasm. Normal

mucous membrane or granulation tissue often overlies the neoplasm so that multiple biopsies of various portions of the lesion may be required to yield an accurate diagnosis.

Additional bronchoscopic information of value is the site and extent of the tumor in its relation to the major bronchi and trachea, and evidence of extensive metastases to the mediastinal lymph nodes as shown by widening of the carina or fixation of the bronchial tree. At bronchoscopy the larynx likewise can be inspected directly for evidence of recurrent laryngeal nerve palsy.

One note of warning might be interjected here in regard to taking a biopsy through a normal and intact mucous membrane. Our own experience includes a case of hemangioma so biopsied, following which there was a profuse gush of blood which filled the bronchoscope and threatened to suffocate the patient until she was suspended in an inverted position over the edge of the operating table and the bleeding ceased spontaneously before exsanguination took place. On another occasion one of us ruptured a non-pulsating aneurysm of the aorta with the bronchoscope with immediate death of the patient. A catastrophy was recently averted when a protruding mass in the trachea was not biopsied because it was covered by normal mucosa, and an aneurysm of the innominate artery was found at exploration, although it was fully expected that a neoplasm would be found. (Angiograms had not been made).

Aspiration biopsy with a needle through the chest wall is intentionally omitted, since there are safer ways of arriving at the diagnosis of a neoplasm in the lung, and the danger of implanting carcinoma cells in the chest wall is pointed out by Dolley and Jones, and others.

Exploratory thoracotomy is now widely used in patients who present strong presumptive evidence of a primary neoplasm of the lung but whose preliminary examinations have failed to yield a positive diagnosis. It is used with the same degree of safety (and with less discomfort to the patient) as is exploratory laparotomy. To wait to see what develops in a patient who offers suggestive evidence of a pulmonary neoplasm is to let the opportunity for cure be forever lost in many instances. Even benign appearing tumors should be explored promptly because many of them are actually malignant, the majority of the others have malignant potentialities, they will eventually produce bronchial occlusion with suppurative complications, and even those most completely benign will (with continued growth) assume a size sufficient to crowd contiguous and vital structures with untimely death of the patient.

Treatment

Until Graham in 1933 performed the first successful pneumonectomy for bronchiogenic carcinoma, such a diagnosis was equivalent to a death sentence to the patient. The literature now contains increasing numbers of patients reported to be alive five or more years after pneumonectomy for carcinoma of the bronchus, and Graham's first case is still alive and well seventeen years later.

The mortality rate incidental to a total pneumonectomy per se has been reduced to a level comparable to that of major abdominal operations. Technical advances in physiology, anesthesiology, blood banking, chemotherapy, antibiotic therapy and thoracic surgery have made invasion of the chest a safe and practical procedure. Accordingly, the mortality rate reported by any one surgeon will depend upon the extent of radical dissection he feels justified in performing.

The objectives of treatment of a patient with bronchiogenic carcinoma are two-fold. The primary desideratum is, of course, complete eradication of the neoplasm and can be accomplished only by means of surgery. When all examinations indicate that the carcinoma is confined to one lung, or to the lung and its regional lymph nodes, total pneumonectomy is the treatment of choice.

The second desideratum of treatment is that of palliation and amelioration of the patient's symptoms when a curative surgical procedure is impossible. This can be accomplished by means of either a limited or extremely radical resection intended to remove the source of the patient's symptoms, or by the use of nitrogen mustard (Methyl-bis) and/or deep x-ray irradiation. It becomes a matter of judgment on the part of the patient's physician which course will provide the individual patient with the longest life and the greatest freedom from discomfort.

Other palliative measures to be employed in cases with extensive and painful infiltration of the chest wall by carcinoma are multiple intercostal neurectomy, high chordotomy or cerebral lobotomy.

It is obvious that the number of patients who will be cured of bronchial carcinoma will depend upon the early recognition of the disease, and the number recognized in time for a curative resection is still distressingly small but improving. Brock in 1938 found only 4 of 106 patients with carcinoma of the bronchus who had no demonstrable extension beyond the limits of the lung. Overholt in 1940 reported 14 of 100 patients whose carcinoma proved resectable, and Churchill in the same year reported 17.4 per cent of 155 patients with carcinoma whose lesions could be completely removed. Ochsner and DeBakey performed resections

upon 195 of 548 patients, but only 57 of these were done with the expectation of a cure, a total of 10.4 per cent. It is encouraging to note that in Ochsner and DeBakey's report of 1948 there were 8 patients alive and well among those 36 who had resections more than *five years* previously, 22.2 per cent of the operated group and 1.5 per cent of the total number with a diagnosis of carcinoma of the bronchus. There were 12 additional living patients in the four year survival group who, if they all survive, would increase the number of five year survivals to 20 in the following year. Additional candidates for long term survival were to be found in the first, second and third year postoperative groups.

It is generally agreed that evidence of distant metastases from a bronchiogenic carcinoma such as are found in the axillary or supraclavicular lymph nodes, brain and liver, are definite indications of inoperability of the tumor. The majority of thoracic surgeons agree that pleural fluid in which neoplastic cells can be demonstrated is likewise a contraindication to surgery.

Evidence of recurrent laryngeal nerve paralysis, phrenic nerve paralysis, Horner's syndrome, brachial plexus involvement, and severe chest wall pain indicate that total extirpation of the carcinoma is unlikely, but do not contraindicate exploration, especially when a positive diagnosis of carcinoma has not been made. Each of these nerves has been found to be affected by pressure from relatively benign tumors, and even when direct invasion by carcinoma has taken place it is possible in many instances to perform a sufficiently radical dissection to relieve the patient of his distressing symptoms. One is likewise justified in performing a resection of a lobe or a lung in which suppuration is present and is the cause of the majority of the patient's symptoms, even when such a resection offers no reasonable hope of cure.

However, it is to be remembered that a person from whom a lung has been removed, particularly a patient in the older age group, is far from being a comfortable person. It is difficult to maintain the heart and mediastinum in the mid-line even with the use of air or plasma in the empty hemithorax, and the retraction of the mediastinum toward the operated side and overdistention of the remaining lung produces discomfort, and often dyspnea, which is continuous throughout the remainder of the patient's life, unless a secondary thoracoplasty is performed. One hesitates to perform a thoracoplasty upon a patient whose life expectancy is limited, adding thereby to the sum total of his discomfort.

For these reasons it is the firm conviction of this Group that resection should be performed: 1) when if offers a reasonable hope of cure or, 2) when it is directed at the alleviation of symp-

toms which are present or are likely to occur within the immediate future.

As has been pointed out by Skinner et al, it is important to the comfort and happiness of a patient with inoperable carcinoma to maintain as high a level of general health as possible. Particular attention is paid to his red blood cells and hemoblobin. He is given a high protein diet, often supplemented with a high protein drink formula, extra vitamins and iron. The following high protein drink formula has proved palatable and effective in helping to maintain blood protein levels, and may be served between meals as a drink or frozen into a sherbet with varying flavors:

6 egg whites,
6 tablespoonfuls skimmed milk powder,
[Starlac (Borden's) or commercial powder],
4 ounces Karo syrup,
6 ounces orange juice, or flavored to taste with chocolate, vanilla, spiritus frumenti, or other flavoring.

The use of nitrogen mustard (Methyl-bis) has produced marked benefit in the reduction of pain and improvement of bronchial drainage in 70 per cent of our cases. The initial experience reported by Skinner et al. has been confirmed in our subsequent observations. The Methyl-bis is given in 10 milligram doses, administered intravenously on four consecutive days. The affinity of Methyl-bis for young cells gives rise to its principle complication of repression of the formation of blood cells and platelets, so that blood counts at bi-weekly intervals following its use are indicated, as are transfusions whenever necessary.

The patient's infectious complications are controlled with the use of antibiotics and a bronchial drainage routine which includes 15 grains of ammonium chloride four times a day as an expectorant, postural drainage at least four times daily and a high fluid intake.

Deep x-ray therapy as applied for palliation and the relief of pain, usually following the course of Methyl-bis, is customarily reserved for such a time as it may be specifically needed.

The effectiveness of this palliative regime is demonstrated by the fact that numerous patients have been able to return to work for periods of a year to two and one-half years, requiring nothing stronger than codeine for occasional sedation up to a short time before their eventual deterioration and death.

Treatment of the superior sulcus tumor of Pancoast deserves special mention because it is usually, but not always, a carcinoma of the bronchus which has extended beyond the limits of the lung. No reports have come to our attention which indicate that a patient has survived five years or more after surgical extirpation

of such a tumor when *carcinoma* was the etiological factor. However, it is now our opinion that these tumors should be explored because occasionally a neurofibroma is found producing the syndrome, even including bone erosion, and can be completely extirpated.

Palliation can also be afforded to some of these incurable patients whose tumor is carcinomatous by resecting the mass and at the same time performing an intercostal neurectomy. It is our practice to fulgerate any tumor tissue left behind, and one such patient of ours has now been working without pain for a period exceeding two years.

Hamartomas and chondromas are relatively benign so that when they are found upon exploration, as limited a resection as possible is indicated In some cases they have been "shelled out" without sacrifice of lung tissue and in others a segmental resection of a portion of a lobe has proved adequate. Their usual peripheral location lends itself to this type of excisional treatment when suppuration and bronchiectasis are absent.

Lipomas which are pedunculated can be removed safely at bronchoscopy by means of the biopsy forceps and can be expected to be cured by this treatment. But when lipomas cause bronchial occlusion, exploration of the chest is indicated with their removal by bronchotomy if possible, or lobectomy if necessary to extirpate them completely and remove bronchiectatic and infected segments peripheral to them.

Fibromas and myoblastomas, being actually tumors with malignant potentialities, require excision with an adequate margin to assure their total removal, and lobectomy is usually necessary, or pneumonectomy if a main stem bronchus is the site of their origin.

Hemangiomas of the bronchus are similarly treated, although we have a patient (mentioned as the one whose biopsy was followed by severe hemorrhage) alive and well without symptoms seven years following a single course of deep x-ray irradiation.

Sarcomas and fibrosarcomas are treated following the principles laid down for any other malignant growth in the lungs; radical and complete extirpation if possible, together with a resection of the regional and mediastinal lymph nodes. The result of treatment in the true sarcoma group is discouraging, none of the six cases accepted by Stout having survived a five year period. None of the patients encountered in our own experience presented an operable tumor at the time they were seen and deep x-ray irradiation produced no appreciable improvement.

Treatment of alveolar cell carcinoma has been unsatisfactory in general, although Graham has mentioned a case in which lobectomy was performed with relief of symptoms for four years,

but eventual death occurred as the result of extension or recurrence in other lobes. In our own experience, a patient revealed alveolar cell carcinoma in a lobe removed for bronchiectasis, but died a few months later as the disease progressed (Case 4). There are no reports to our knowledge of x-ray irradiation having proved of material benefit to these patients and no series treated by Methyl-bis has been reported.

Case 1: Mr. B.J.A., age 51, white male. This patient's history is included to illustrate a rather large group of patients whose diagnosis is delayed unduly while the infectious complications are being treated by the entire gamut of chemotherapy and antibiotics.

C. C.: Fever, cough, sputum and weight loss beginning five months previously.

P. I.: About the First of September 1949, the patient began to be aware of a low grade fever, a gradually increasing cough with sputum, and an insidious weight loss. No acute illness was recalled. During the following months until January 20, 1950, the patient received treatment with a succession of antibiotics until all of them available on the market had been given a thorough trial. This resulted in some marked gain in the

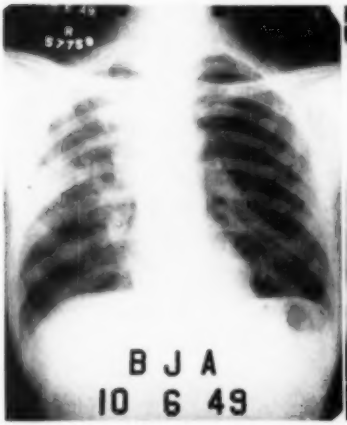
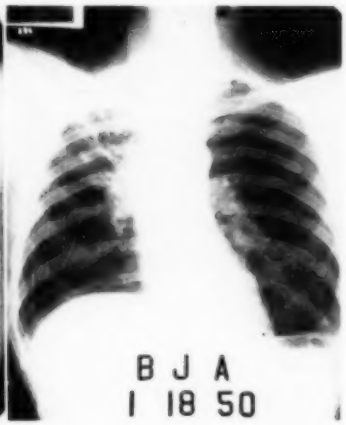


FIGURE 1



(CASE 1)

FIGURE 2

Fig. 1, Case 1: Mr. B.J.A. (Bronchiogenic carcinoma), October 6, 1949. The chest film suggests the presence of a pulmonary tuberculosis or "virus pneumonia" involving the upper two-thirds of the right lung, with a suggestion of some enlarged hilar ndoes on this side. On the left there is some minimal infiltrate in the extreme apex.—*Fig. 2, Case 1:* Mr. B.J.A., January 18, 1950. During the interval between these two films, this patient has had numerous antibiotics which have apparently brought about some improvement in the pneumonitis in the right lung. Some of this clearing may actually represent a contraction of the lobe rather than resolution. The right hilar mass is more definite at this time, and a bronchoscopic biopsy revealed the presence of an unclassified bronchogenic carcinoma with tracheal involvement. We see therefore that carcinoma patients can improve temporarily *and deceptively* with antibiotics.

patient's weight, but without full return of his strength. A mild cough persisted with sputum occasionally streaked with blood. Wheezing and dyspnea had developed in the meantime.

P. H.: The past history was essentially non-contributory.

P. E.: The patient was a poorly nourished white male appearing chronically ill. There was a subicteric tint of the skin with multiple pigmented nevi over the chest posteriorly, some of which appeared irritated and suggested the possibility of a malignant melanoma. The veins over the neck, chest and abdomen were distended.

Examination of the chest showed limited motion on the right with wheezes, rales and ronchi over the upper half of the right lung field.

The remainder of the general examination was not remarkable.

The laboratory reported the blood counts within normal limits and the blood sedimentation rate, corrected for cell volume, was elevated to 34 mm. in one hour.

X-ray films of the chest made on January 18, 1950 were compared with earlier outside films made in September 1949. There was noted considerable clearing of a diffuse infiltrate present in the upper third of the right lung, some of which may have represented a contraction of the lobe rather than a true resolution of the infiltrate. There was an increase in the size of the right hilar shadow and in the lateral view a density was visible about 5.0 x 8.0 cm. in diameter.

Fluoroscopic examination revealed the right diaphragm paralyzed and elevated and it exhibited paradoxical motion on sniffing.

Bronchoscopic examination on January 20, 1950 revealed a tumor at the lower end of the trachea which was granulomatous and partially obstructing the lumen of the trachea itself, leaving a lumen not over 5.0 mm. in diameter. Inspection beyond this point was impossible.

A biopsy was taken from the tumor in the trachea and was reported as bronchiogenic carcinoma, undifferentiated.

Because of the obvious tracheal involvement surgery was not recommended, but instead the patient was given a course of Methyl-bis intravenously which was followed by deep x-ray irradiation. Six weeks later the patient showed marked improvement of his wheezing and dyspnea, and the blood had disappeared from his sputum.

Case 2: Mr. G.S., age 45, white male. This case has been selected to illustrate the close clinical resemblance between some cases of carcinoma of the bronchus and pulmonary tuberculosis. All routine examinations indicated a diagnosis of pulmonary tuberculosis except for the absence of tubercle bacilli in the sputum.

C. C.: Hemoptysis five weeks previously.

P. I.: The patient complained of a spasmodic cough of fifteen or twenty years duration, and two years earlier had been studied at the Arkansas State Tuberculosis Sanatorium for two weeks where sputum examinations were negative for tubercle bacilli and where x-ray examinations apparently showed no active tuberculosis.

Two months before admission to the Baptist Memorial Hospital the patient had pneumonia, and approximately one week after recovering from this he raised one teaspoonful of blood in his sputum. The blood gradually disappeared and at the time of admission his sputum consisted of about one tablespoonful of clear mucus daily. Wheezing had appeared two months earlier and was constant, and the patient complained of easy

fatigue and only a fair appetite. He had no fever, no chest pain or night sweats. Weight loss was moderate.

P. H.: The patient's only significant illnesses previously were five attacks of pneumonia since 1916. There was no known tuberculosis contact.

P. E.: The patient was well developed and fairly well nourished with a temperature of 99.0 degrees F., pulse 80, blood pressure 122/84. The general examination was non-contributory except for a scar in the left posterior axillary line where an old empyema had been previously drained. The lungs were essentially normal to physical examination and no rales were heard.

The chest x-ray films made on August 11, 1945 revealed in the right lung a cavity measuring 2.5 cm. in diameter in the right infraclavicular area. There was likewise a small amount of flocculent infiltration in the first interspace peripherally. The left lung was clear. There was some pulmonary emphysema revealed in both bases and the right costophrenic angle was blunted while the left diaphragm was flattened and adherent to the chest wall laterally. X-ray impression was chronic fibroid cavernous pulmonary tuberculosis, bilateral pulmonary emphysema, and possible tracheobronchial tuberculosis.

The laboratory reported the blood counts within normal limits and the blood sedimentation rate corrected for cell volume at 15 mm. in the first hour.

Because of the patient's wheezing a bronchoscopic examination was performed on August 20, 1945 and some granulation tissue with an ulcer

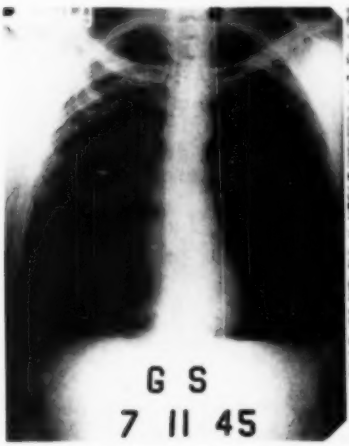


FIGURE 3 (CASE 2) FIGURE 4

Fig. 3, Case 2: Mr. G.S., July 11, 1945. The chest film here suggests a typical pulmonary tuberculosis with a right infraclavicular cavity measuring about 4 cm. There is very little parenchymal reaction around the cavity, and there is a suggestion of enlarged calcified nodes on the left. The final diagnosis in this case was epidermoid bronchiogenic carcinoma, inoperable.—*Fig. 4, Case 2:* Mr. G.S. Biopsy specimen from granulation tissue in the trachea under low power reveals a fairly rapidly growing epidermoid carcinoma, Grade III. Numerous mitotic figures are seen and the individual cells vary greatly in size and staining characteristics.

was found at the orifice of the right upper lobe bronchus. This granulation tissue extended up the right wall of the trachea about 1.0 cm. A specimen was removed with the biopsy forceps and revealed epidermoid carcinoma, Grade III.

Since the pathologic report did not agree with our clinical impression, the bronchoscopy was repeated September 8, 1945 and the fungating mass was now seen to be larger than before. It was attached along a broad base on the right wall of the trachea. Biopsy specimens were again removed and again revealed epidermoid carcinoma.

Because of the extensive tracheobronchial involvement no resection was undertaken and only palliative treatment was advised.

Case 3: Mrs. A.C.G., age 58, white female. This patient was first seen at the John Gaston Hospital on March 12, 1945.

C. C.: Fever, chest pain and a productive cough.

P. I.: In the hospital she had fever for three days, with some pain in the left costal margin. X-ray examination of the chest made the day after admission showed an increase in the hilar glands bilaterally with an area of consolidation at the left base. The patient was placed on one of the sulfa drugs. X-ray film of the chest on March 22, 1945 showed a decrease in the density. The discharge diagnosis was tonsillitis and acute interstitial pneumonitis. She was discharged home on April 5, 1945. She was re-x-rayed as an out-patient on April 14, 1945 which showed "post-pneumonic fibrosis."

The patient was apparently free of symptoms until shortly before her second admission on February 4, 1947. At that time she was running a temperature of 104 degrees F., complaining of cough with a small amount of purulent sputum. There was some leukocytosis. X-ray findings on admission were reported as pneumonia of the left lower lobe. X-ray film on February 12, 1947 showed more extension and then on February 21, 1947 showed some clearing. She was discharged on February 24, 1947 with a diagnosis of bronchopneumonia.

The third admission was on June 7, 1947 at which time she was admitted complaining of fever, cough, sputum and pain in the left chest. X-ray examination on admission showed a patchy infiltrate at the left base. She was not running much fever at this time, and the diagnosis of primary atypical pneumonia was made. On June 13, 1947 an attempt was made to secure bronchograms by instillation of iodized oil, and some bronchiectasis was demonstrated in the left lower lobe. On June 17, 1947 the patient was bronchoscoped by the Ear, Nose and Throat Service, at which time only a slight increase in the mucus coming from the left lower lobe was seen. This sputum was examined for tumor cells but none were found. The patient was discharged home on June 21, 1947.

Her next admission was on February 8, 1948 when she was readmitted because of fever and chest pain. X-ray film on February 9, 1948 showed a moderate extension of the previously described infiltrate in the left lower lobe, and it was diagnosed as a bronchopneumonia. Subsequent films on February 13, February 22 and March 10, 1948 showed no change. Bronchograms were repeated on March 17, 1948 and showed a definite though moderate bronchiectasis apparently limited to the left lower lobe. The patient was bronchoscoped again on March 24, 1948, at which time the mucous membrane was seen to be reddened from the level of the vocal cords on down. There was a moderate amount of purulent sputum in both lower lobes, with an increased amount in the left lower lobe.

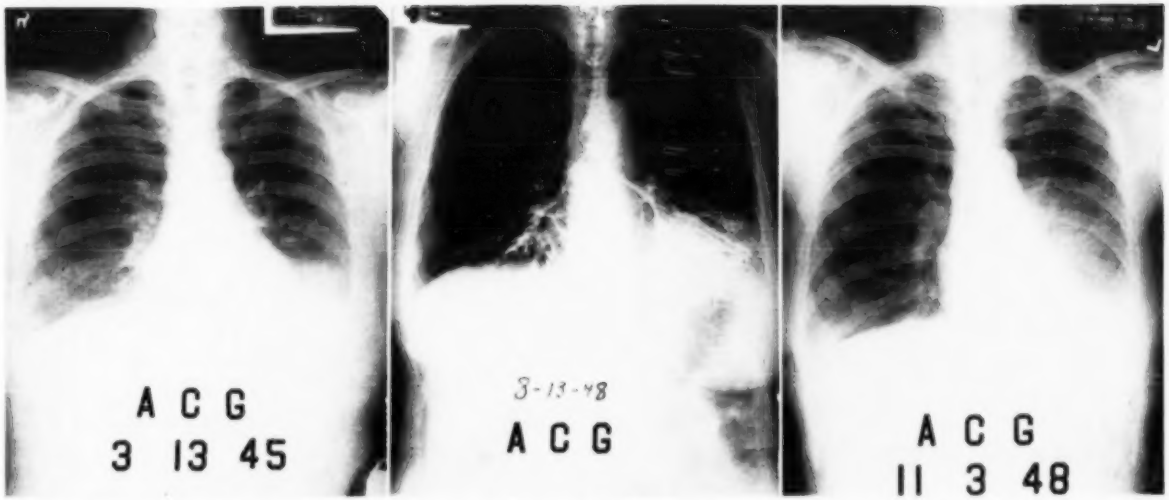


FIGURE 5 (CASE 3) FIGURE 6 (CASE 3) FIGURE 7 (CASE 3)

Fig. 5, Case 3: Mrs. A.C.G. (Alveolar Cell Carcinoma), March 13, 1945. This patient was repeatedly hospitalized for attacks of bronchopneumonia which always localized in the left lower lobe. It was during such an attack that this film was made and there is a definite infiltration in the left base with slight elevation of the left leaf of the diaphragm. The remainder of the lung fields is essentially clear.—*Fig. 6, Case 3:* Mrs. A.C.G., August 13, 1945. Bronchographic studies revealed the presence of a bilateral basal bronchiectasis, most noticeable in the left lower lobe where there was irregularity in the diameter of the bronchi, with some widening and loss of finer branches. No bronchial obstruction was visualized.—*Fig. 7, Case 3:* Mrs. A.C.G., November 3, 1948. Another attack of "bronchopneumonia" again brought the patient to the hospital. Again the bronchopneumonia process was localized in the left lower lobe, but there was a somewhat differential distribution than on the film made three years previously. Suggestion of minute areas of infiltrate in the right base is also seen.

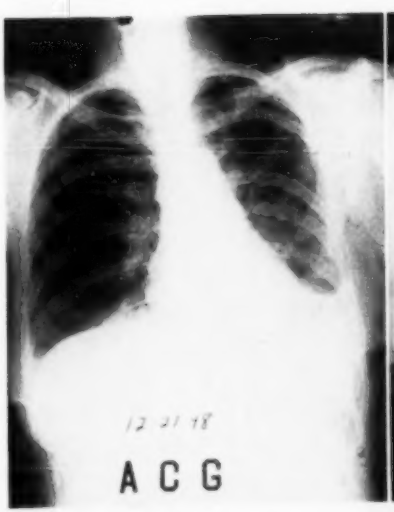


FIGURE 8 (CASE 3)

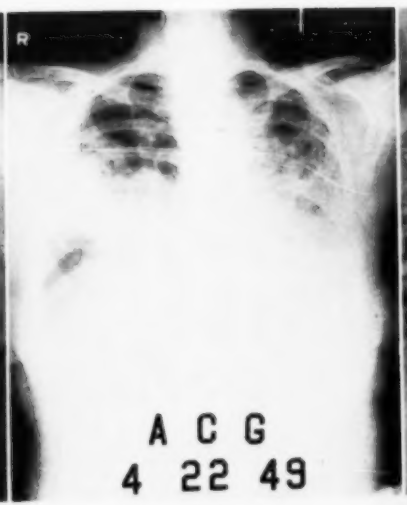


FIGURE 9 (CASE 3)

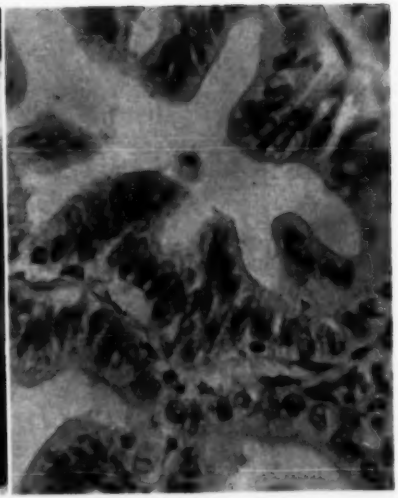


FIGURE 10 (CASE 3)

Fig. 8, Case 3: Mrs. A.C.G., December 21, 1948. A left lower lobectomy was performed and the immediate postoperative course was marred by a slight increase in the "bronchopneumonia" in the right base. Pathological examination of the resected lobe revealed an "adenomatosis."—*Fig. 9, Case 3:* Mrs. A.C.G., April 22, 1949. This film was made shortly before the patient's death, and shows a diffuse spread of the adenomatosis to nearly all of both lungs. This is now classified as an alveolar cell carcinoma.—*Fig. 10, Case 3:* Mrs. A.C.G. A section of the tumor in the left lower lobe under the high power reveals a tumor with polypoid projections obliterating all remnants of normal alveoli. The alveolar type of cell is bazarre, and exhuberant growth characteristics are evidenced by the rather beautiful infoldings and delicate patterns formed by the cells as they push their way into the alveolar lumina.

Secretions were taken for study for tumor cells, and the report was obtained that the sputum contained "many fat-laden macrophages." The patient was discharged home again on March 27, 1948.

She was readmitted on October 10, 1948 with a diagnosis of a chronic interstitial pneumonitis and bronchitis. X-ray film on October 10, 1948 showed no change from the previous films. Because of the repeated bouts of pneumonia and the demonstrable bronchiectasis, the patient was transferred to the thoracic surgical service on October 24, 1948 with the idea of doing a lobectomy if possible. X-ray film on October 25, 1948 showed some extension of the infiltrative process. Patient was bronchoscoped on November 18, 1948 and a large amount of purulent sputum was seen in the left lower lobe bronchus. On November 29, 1948 the patient was taken to surgery and left thoracotomy was done. At that time the left lower lobe and the lingula of the left upper were found to be completely atelectatic. They were lightly attached to the surrounding structures by fibrinous adhesions which were easily divided. The lower lobe and lingula of the upper lobe were removed by the individual ligation technic, and the immediate postoperative condition of the patient was good. The remaining lobe on that side expanded without difficulty with the use of an intercostal tube and underwater seal. On December 1, 1948 the postoperative film showed satisfactory reexpansion of the left lung and a clear right lung. Subsequent films on December 6 and 13, 1948 showed that the lung fields were in a satisfactory state. The pathological report on the resected lung tissue was pulmonary adenomatosis. On January 7, 1949 x-ray examination of the chest showed some infiltrate in the upper lobe on the left and subsequent films showed that this process spread to the right base, as well as becoming more extensive on the left. About the middle of January 1949, the patient began to complain of some shortness of breath and began to raise large amounts of clear mucoid sputum. This amount of sputum gradually increased and the shortness of breath increased, in spite of bronchial drainage measures to help keep the bronchial tree clear. The patient was discharged home, however, on February 25, 1949 with the family understanding that the pulmonary adenomatosis had already spread and the patient's eventual outlook was hopeless. The patient was followed in the out-patient department by periodic x-ray films which showed a gradual but progressive increase in the infiltrative lesions in both lungs. On April 5, 1949 the x-ray department asked permission to start some x-ray therapy to the chest to see if the spread of the adenomatosis could be checked, and the patient received 1,000 r through air to an anterior and posterior port over the left lung between April 5 and 14, 1949. There was no improvement in the patient's symptoms during this course of therapy.

The patient was admitted again to the John Gaston Hospital on April 25, 1949 because of the increasing shortness of breath and increase in sputum. There was no pain. Examination showed coarse rales over the left lung with dullness. Her course was one of gradual decrease in strength. The patient continued to raise large amounts of clear mucoid sputum, as much as 500 cc. for 24 hours, and died on May 19, 1949. Permission for autopsy was not granted.

SUMMARY

The pathology, clinical diagnosis and treatment of the various primary pulmonary neoplasms is discussed.

A list of these tumors encountered in our practice and gleaned from the literature is presented and the principle pathologic characteristics of each is described. The actual or potential malignancy of almost all of them is emphasized.

An attempt is made to stimulate the physician's suspicion of the presence of a bronchial or pulmonary neoplasm early in the disease, and a routine of examinations is proposed to reveal the diagnosis as early as possible. Special factors to be observed during the course of the examinations are mentioned. The manner in which carcinoma of the bronchus may simulate pulmonary tuberculosis or "virus pneumonia," or be masked by associated pulmonary suppuration, is emphasized, and examination for bronchial neoplasms is urged before a long time is expended applying the many chemotherapeutic and antibiotic drugs.

The extent of resection necessary for the complete extirpation of the various primary pulmonary neoplasms is discussed, and measures to make life more endurable for those patients whose tumors are inoperable are described.

Illustrative case histories are presented, and one new case of alveolar cell carcinoma of the lung is reported.

RESUMEN

Se discute el diagnóstico anatomo-patológico, el clínico y el tratamiento de los tumores primarios pulmonares.

Se presenta una lista de los tumores encontrados en nuestra práctica y referidos en la literatura y se describen las características de cada uno. Se recalca la malignidad presente o la potencial de todos ellos.

Se intenta estimular la sospecha del clínico acerca de los tumores pulmonares, de manera temprana y se propone una serie de exámenes de rutina para ese diagnóstico oportuno. Se mencionan los factores especiales que se observan durante la investigación.

Se insiste en la manera como el carcinoma puede simular la tuberculosis pulmonar o la "neumonía de virus" y puede enmascararse por la supuración y se hace énfasis en la necesidad de investigar las neoplasias bronquiales antes de que transcurra mucho tiempo empleando las numerosas drogas químicas y antibióticas.

Se discute la extensión de la resección necesaria para la extirpación completa y se describen las medidas que han de tomarse para hacer la vida más duradera y soportable a los inoperables.

Se presentan historias clínicas demostrativas y se presenta un nuevo caso de carcinoma de células alveolares del pulmón.

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Benign Tumors of the Lungs with Special Reference to Adenomatous Bronchial Tumors

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Today adenomatous tumors of the bronchi are well known as a pathological and clinical entity and much of the confusion to be found in the literature from 1850 to 1932 has been dispelled by numerous later publications[1-40] (Fig. 1). The nomenclature, pathogenesis, histology, relation to bronchiogenic cancer, differentiation from other polypoid tumors (Fig. 2), symptomatology, surgical management, and other forms of treatment have all been thoroughly reported upon. Controversy still exists in some points of treatment and pathogenesis. In spite of the recent frequent reports it would appear timely to present an up-to-date concept of adenomatous tumors of the bronchi. There will also be described two variants of bronchial adenoma not usually considered a part of this group. This concept includes unpublished observations and deductions bearing on the present status of pathogenesis, biological life history, and especially relation with similar tumors arising elsewhere in the body.

To understand the present status of comparable adenomatous tumors arising in the mixed glands of the trachea and bronchi (Fig. 3), one has only to recall the long and uncertain history of so-called mixed tumors of the salivary glands. Many years ago they were called cylindromas and then for a long time there was endless discussion as to whether they were epithelial or endothelial or of several germ layer origin. Now, most pathologists are content to call them mixed tumors, recognizing at the same time that they are not mixed from the embryological point of view but that this term has such definite clinical and pathological connotations that to change the name, though probably wrong, would augment

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Completion of the original paper was interrupted by the untimely death of Professor Conner in 1946. The present paper is the result of additional material being added since that time.

confusion. From the many different names[7] and descriptions given to adenomatous tumors of the bronchi it is obvious that some agreement must be reached as to their histogenesis, histological variations, and ultimate behavior. At the present time we recognize four histological and clinical variants which make up the adenomatous bronchial tumors. In order of decreasing malignant qualities they are: (1) mixed tumor (Fig. 4, Case 12) (cylindroma) (Fig. 5, Case 32); (2) carcinoid (Figs. 8, 8A, 9); (3) myoblastoma;[41] (4) benign glandular (Fig. 6, Case 35).

The name cylindroma is generally attributed to Billroth[41] (1856), who described them as occurring in the salivary and lacrimal glands, the paranasal sinuses and the pharynx. Koester,[42] (1867), may have been the first to start perpetuating this term when he described two cases, one in the neighborhood of the sublingual gland and one from the orbit as "Kankroid mit hyaliner degeneration" (Cylindroma Billroth's). That Billroth did not know then what kind of tumor he was dealing with (we say this without derision, acknowledging our own inadequacy) is shown by a later report,[44] in which he states: "I have seen more recent tumors with a papillary formation arising from mucous membrane resembling cylindroma; this formation is not so characteristic as I thought at first, as they occur in sarcomas as well as in adenomas and carcinomas." Omitting many references one comes to von Dembowsky,[45] (1891), describing such a tumor of the skin as a chondroendothelioma,* and another case of so-called cylindroma of the nose which he called epithelioma microcysticum with invasion by an angioma myxomatoides. This latter, according to von Dembowsky, belonged to the mixed tumors. His pictures resemble basal cell epithelioma in some places, and the usual salivary gland tumor in others. But Marchand,[46] (1893), described a tumor of the antrum of Highmore as an endothelioma with hyaline cylinders. One felt, however, that as more became known about physiological and histological differentiation of cells that we might allow epithelial cells to form a wide variety of tissues including a mucin which differs very little in appearance or chemical composition from chondromucin, round cell or spindle cell carcinomas in which fibrils can be demonstrated, while considering also the contrary fact, that many kinds of epithelium, and so carcinomas, arise from mesodermal structures.

Snellmann,[47] (1931), reviewed the origin and histology of so-called mixed tumors of the large salivary glands and illustrated spindle shaped epithelial cells and reticular epithelial tissue re-

*This is exactly like the tumor reported by L. C. Simard, "Tumor of the Palm Having the Structure of a Mixed Tumour of the Salivary Glands."[48]

sembling endotheliomas in different parts of mixed tumors. He described and illustrated fibrillary structures which formed a reticulum when impregnated with silver and showed reticulated epithelial cells. He described the process of cartilage formation in these tumors and concluded that there are tumors in which the epithelial cells are differentiated morphologically and functionally into different types so that they resemble certain of the mesenchymal cells. The mixing of epithelium and mesenchymal-type cells forms a tissue which has the appearance of being mixed (Fig. 3). His article contains references to discussions as to whether these tumors are mixed tumors, endotheliomas, or epitheliomas, and his reasons for assuming them to be of epithelial and not mixed-cell origin seem convincing. So, too, do the pictures and reasoning of Simard,[48] (1938), for deciding that the tumor with many mixed elements in it which arose in the palm of the hand was probably of sweat gland, almost certainly of epithelial origin. This contains distinct epithelial elements, mucinous degeneration, cartilage and bone. It seems highly probable that the so-called chondromas, chondrosarcomas, and chondroepitheliomas of the breast are derived from accessory skin glands. This is strikingly brought out by Allen,[49] (1940), who describes transitional stages in the development of cartilage from epithelium in breast tumors.

FIGURE 1

HISTORY OF BRONCHIAL ADENOMA AS NEW CLINICAL ENTITY

1. Post Mortem Recognition, 1882 to 1932:	
Müeller	1882
Horn	1907
Patterson	1930
Reisner	1928
Geiple	1931
2. Bronchoscopic Recognition and Treatment, 1930 to 1939:	
Kramer	1930
Wessler and Rabin	1932
Kernan	1935
Kramer and Som	1935
Jackson and Konzelman	1937
3. Newer Knowledge and Future Treatment, 1938 ——	
Hamperl	1937
Wamach and Graham	1938
Brock	1938

This chart depicts three stages of historical development with a few pertinent references. Stage 3 (therapeutically) is characterized by the recognition that pulmonary resection, lobectomy and pneumonectomy, is the ideal treatment, with transpleural bronchotomy and bronchoscopic removal reserved for only very selected cases.

He states, with reasons, that the term mixed tumor applied to neoplasms of the breast which have epithelial elements along with cartilage or bone is misleading and if used at all should be reserved for tumors composed of dysontogenetic tissues such as organoid teratomas. The tumors then which he describes coming from breast glands, would seem to be closely related to tumors of sweat gland origin, which may form cartilage or bone or both. This is saying again, what we have indicated above, that the presence of cartilage or bone does not imply an origin from embryonic rests or from more than one germ layer. As such tumors are much more common in the salivary glands they have been much more extensively studied. Fry,[50] (1927), and others[51,52] have agreed in general with Snellman. We believe the time past when a tumor, because it may develop some bone or cartilage, must be called a mixed tumor of cellrest or teratomatous origin. The late James Homer Wright[53] called the latter "bastard cartilage" and recognized clearly its illegitimate origin. In 1938, Swinton and Warren[54] renew this ancient controversy and conclude that salivary gland tumors of the mixed type ought to arise from embryonic rests because of their extraordinary variability in histological appearance. Whether or not any of these tumors is mixed or an adenoma of peculiar behavior characteristics is of much less importance than to recognize them as a group and to determine their natural history. Unless a common name is decided upon the literature will remain confused and proper decisions cannot be made as to their treatment.

By drawing upon observations made over the past twenty years from a large series of patients with adenomatous tumors of the bronchi (See Table of Cases), whose clinical course, histology,

FIGURE 2

AGE OF INCIDENCE — BRONCHIAL ADENOMA

	No. of Patients	
1 to 10 years	1	5.5%
11 to 20 years	1	5.5%
21 to 30 years	4	22.0%
31 to 40 years	6	33.0%
41 to 50 years	6	33.0%

SEX INCIDENCE — BRONCHIAL ADENOMA

	No. of Cases	Per cent of Total
Females	10	56.0
Males	8	44.0

Only the first 18 cases appear on this chart but these statistics are applicable to the entire group of 38 cases. Note the contrast with bronchogenic carcinoma where 90 per cent are males and over 70 per cent occur after the age of 50 years.

and successful response to therapy separated them sharply from the usual fatal bronchiogenic carcinoma, it is the purpose of this paper to present a concept which will place the adenomatous bronchial tumors in relationship to other tumors of similar behavior found in the skin, oro-pharyngeal mucous membrane, gastrointestinal tract, and other gland bearing areas such as the parotid glands. It is further proposed that this group of adenomatous bronchial tumors has numerous histological variants to which we wish to add in this paper some new observations (recognizing that still unobserved possibilities may exist). This concept embraces a point of view that the epithelial cell of the serous and mucous glands, or the ducts of these glands, form the origin of these tumors and that these epithelial cells have the growth potential to develop all grades of benignancy and malignancy as well as to differentiate histologically into tissues of mesenchymal types (Fig. 4, Case 12). And so it is believed that the concept to be described will aid in the understanding of the peculiar behavior characteristics of these tumors as well as to make it possible to develop more rational forms of therapy.

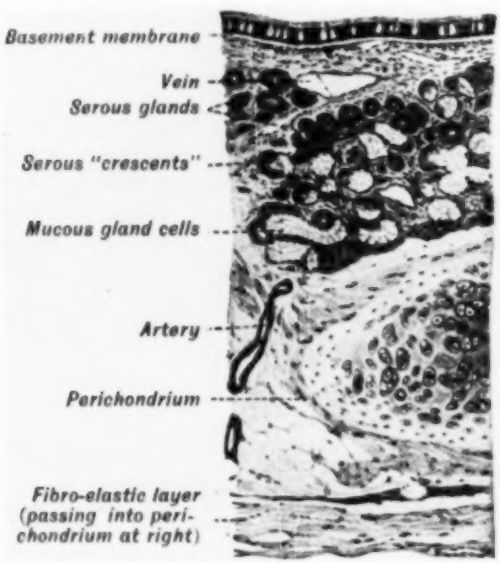


FIGURE 3: Note the two types of glandular epithelium, clear serous and dark mucous secreting cells, which form the mixed glands of trachea and bronchi. The origin of adenomatous bronchial tumors is from the epithelium of these glands and their ducts.

The glands of the trachea and bronchi are not, as we frequently call them, mucous glands, but contain both mucous and serous cells and resemble the accessory glands of the mouth, pharynx, nasopharynx, and the lacrimal apparatus (Fig. 3). Moreover, they originate from downgrowths of epithelium which itself originates in the pharyngeal pouch and it is to be expected that bronchial glands might produce tumors similar or identical to those arising in other glands from the pharyngeal pouch. In this connection mixed mucous and serous glands have been found to be associated with mixed tumors of the parotid gland. It can be shown as well that all these glands have similar physiological properties and may be activated or inhibited by similar substances through the sympathetic nervous system or by central stimulation of that system. But to go into this further, beyond pointing out that similarity, would be a digression outside the scope of this paper. It merely lends more proof, if more is needed, that this preliminary discussion is relevant to the subject at hand.

It would not be practical, if possible, to refer to the ultimate article describing adenomatous tumors of the trachea and bronchi. Nevertheless three periods (Fig. 1) of definite distinction of these tumors from carcinoma have been recognized and the first of these is characterized by the publication of Mueller[55] in 1882, Chiari[56] in 1883, Horn[57] in 1907, Kregliner[58] in 1913, and Malkwitz[59] in 1922. While in general this first period might be termed a period of postmortem recognition, since before the turn of the century bronchoscopy was unknown, there were isolated instances of successful bronchoscopic and surgical therapy reported during the period from 1882 to 1932 when Wessler and Rabin[1] made their

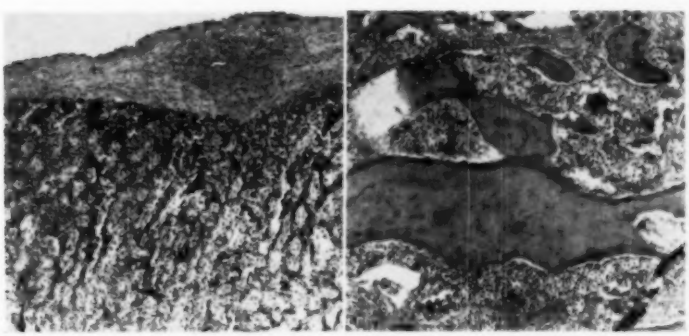
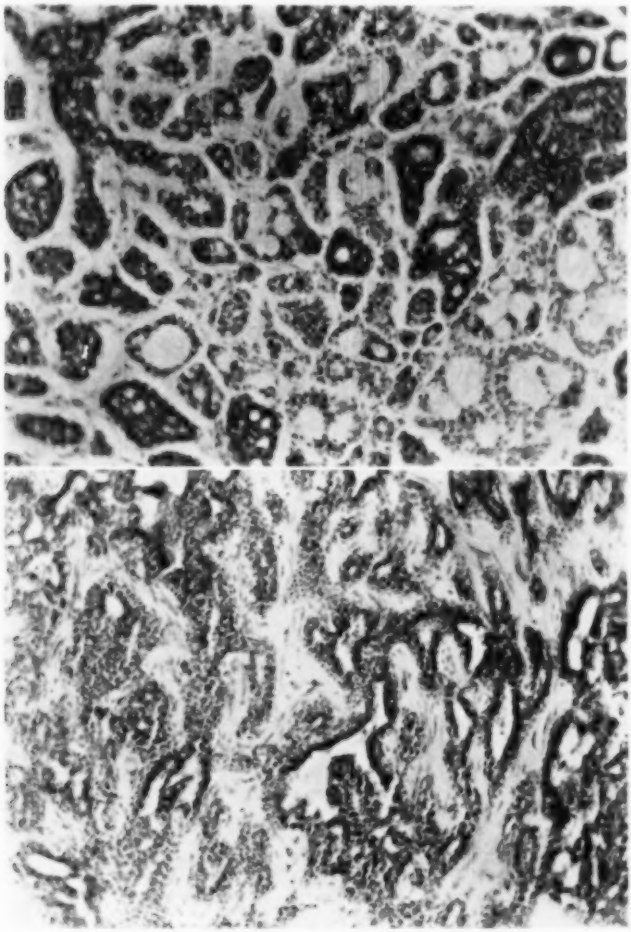


FIGURE 4. Case 12: G.D. Two sections from the same tumor, the gross picture of which is shown in Figure 15—Sections from surgical specimen removed by left lower lobectomy. Note the bone formation, muco-epithelial stroma, and the mixed tumor type of pattern. Total duration 20 years, alive and well 9½ years after lobectomy. Same case as Figures 7 and 15.

report based largely on bronchoscopic and clinical observations (Fig. 7, Case 12). For example, at a meeting of the Medical and Chirurgical Faculty of Maryland, 1904, Dr. Rosenheim[60] reported



FIGURES 5 AND 5A

Figure 5, Case 32: A.H. Tumor removed through a bronchoscope from subcarnial area. Duration 6 years. These different fields from the same section and show, above (Fig. 5), the pattern of a "mixed" tumor of a salivary gland, and below (Fig. 5A), an adenoma with a mucous connective tissue type of stroma. This is usually called mixed tumor or cylindroma, but cystic basal cell epithelioma is probably a more accurate description. Patient expired of asphyxial symptoms with local metastases 6½ years after onset. Radiation and bronchoscopic treatment.

a tumor of the trachea which caused difficult breathing in a woman of 23 years. This was removed by Dr. Halsted after tracheotomy. The tumor was encapsulated and contained mucus. The pathological diagnosis was colloid fibroadenoma. Henrici,[61] (1905), described a tumor of the trachea in a man of 61 who had had asthma for fifteen to twenty years. The pathological description by Ricker mentioned networks of capillaries with hyaline walls, "a cylindroma," lying between which were medium sized cells without intercellular substance. "Mostly it resembled a mixed tumor of the parotid or salivary gland." Again, in 1908, Kreig[62] reviewed primary tumors of the trachea among which were 5 adenomas. He reviewed and described 7 "intratracheal strumas." These were supposed to be adenomatous growths resulting from aberrant thyroid tissue. Jackson,[63] in 1917, reported the bronchoscopic removal of an endothelioma of the right bronchus, a tumor which probably belongs to this group of adenomatous bronchial tumors. Ephraim, in 1917, and Orton,[64] in 1924, described successful treatment bronchoscopically of so-called carcinoma of the bronchus.

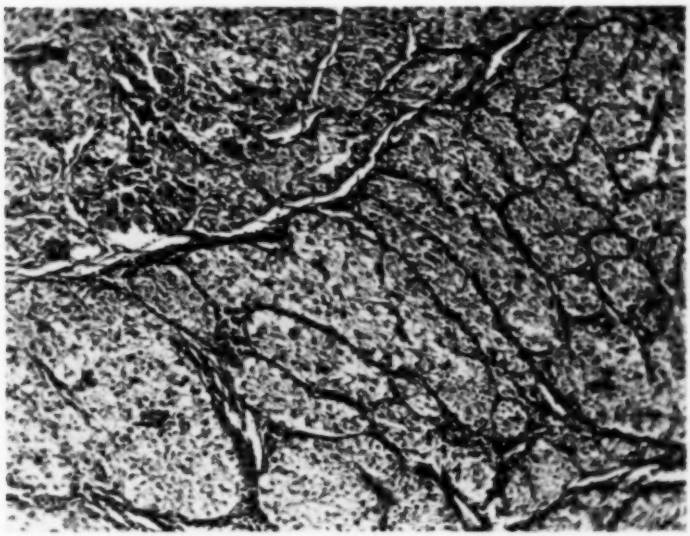


FIGURE 6. Case 35: A.P., female, age 14. Early adenomatous bronchial tumor glandular type. Microphoto showing solid glandular pattern of the sero-mucous glands. Groups of cells with small dark staining nuclei tending to differentiate into myoepithelium at the periphery of cell masses and along the septa. x 150 (from surgical specimen removed at transpleural bronchotomy. Sections are similar to clear cell papillary cystadenoma of salivary glands (Bauer). Total duration 2 years, alive and well one year after bronchotomy. Same case as Figs. 18 and 19.

Other pertinent reports are: Jones,[65] (1918), an apparent cure of an endothelioma or sarcoma of the trachea with radium emanations; Freudenthal,[66] (1918), a recurrent teratomatous tumor of the trachea called a myxo-chondro-cylindroma or endothelioma by J. H. Globus; Lynch,[67] (1929), a mixed tumor of the parotid type growing from the posterior aspect of the thyroid cartilage; Pfeiffer,[68] (1929), five benign tumors of the lower air passages, two of which were called chondromas, three fibromas; and Kramer,[2] (1931), makes one of the first reports of adenomas of the bronchi and claimed that they arose from the ducts of the mucous glands. Patterson,[69] in 1930, reviewed so-called benign bronchial tumors. D'Aunoy and Zoeller,[70] in an uncritical review reported an adenocarcinoma of the trachea and recorded the number of tracheal tumors in the literature up to 1931. These included fibromas, papillomas, chondromas, osteomas, adenomas (a total of 8), lymphomas, intratracheal goitres (25 of them), mixed tumors (2), angiomas (2), and one cylindroma. While it is unreasonable to question the actual occurrence of all these types of tumors, not having seen them, it does seem reasonable to suggest in view of the variable appearance of the adenomas we have seen and the further review which follows that many of these may have been variants of adenomas.

Paul,[71] (1931), called a tumor which caused bronchial stenosis a polypoid angiomyxochondroma; Wessler and Rabin,[1] (1932),

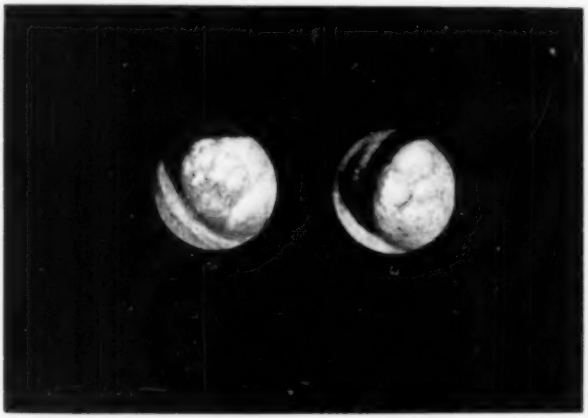


FIGURE 7. Case 12: G.D. Artist's drawing of bronchoscopic views of adenomatous bronchial tumor, mixed tumor type, in the left lower lobe. Only the tip of this 7.0 cm. tumor is bronchoscopically visible, the larger extrabronchial portion, like the submerged portion of an iceberg, is invisible. Duration at time of this prelobectomy bronchoscopy $10\frac{1}{2}$ years. Alive and well $9\frac{1}{2}$ years after lobectomy, total duration 20 years. Same case as Figures 4 and 15.

called 12 of 14 bronchial tumors adenomas, but at the same time they recognized malignant variants; while Campos,[72] (1935), reported a mixed epithelial and cartilaginous tumor in the hilar region of the lung. However, in this year 1935, the name adenoma became better recognized and there were reports by Kramer and Som,[17] Miller,[73] Rosenblum and Klein,[74] of some 26 tumors altogether, recognized as epithelial and adenomatous in nature. In 1936, Morlock and Pinchin[31] said that adenomas were the commonest benign tumors of the bronchi, followed by fibromas and inflammatory polyps, while Peterson[25] observed that there had been 52 cases reported, including 9 of his own. He stated that adenomas made up approximately one half of all benign bronchial tumors but did not say what the other 50 per cent may be. Still Clerf and Crawford[32] in a report before the American Association for Cancer Research preferred to call them benign glandular bronchogenic tumors rather than simple adenomas. They reported 16 tumors composed of columnar or transitional epithelial cells frequently forming acini and pseudo-rosettes. Their structure suggested a mucous gland origin. In the discussion Weller mentioned the difficulty in diagnosis of these tumors from a biopsy, Ewing[75] stated that this is a variable group of tumors which should be separated from malignant bronchial and pulmonary carcinomas.

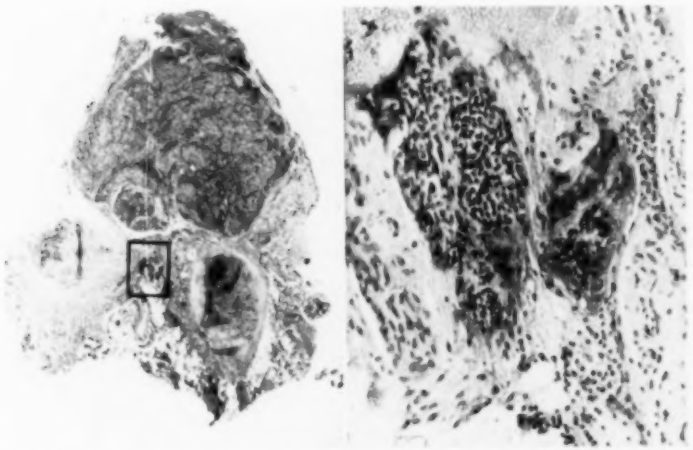


FIGURE 8. Case 34: S.S., age 37. Low power microphoto of adenomatous bronchial tumor, carcinoid type, showing sessile attachment of surgical specimen removed at transpleural bronchotomy from right subcarinal area. Note the cartilaginous rings removed with attached tumor. Higher power microphoto of tumor invading the intercartilaginous area of the bronchial wall taken from area marked by square in low power microphoto. This tumor area could not have been removed via the bronchoscope. Same case as Figures 20 and 21.

He would have classified some as benign adenomas, but others as adenocarcinomas because they seemed to be infiltrating.

What is the present status of the benignancy or malignancy of these tumors? Adenomatous tumors of the bronchi are very similar to mixed tumors of the parotid glands in this regard. The analogy presented by Willis[76] for mixed tumors of the parotid glands as to their innocence or malignancy, and brought out by Womach and Graham[3] for bronchial adenoma, has been corroborated by our own observations in the series of cases presented herein.

Because of their slow growth, their supposed encapsulation and the behavior of metastasis, the adenomatous bronchial tumors have often been classed as "benign." This fallacious idea cannot be too strongly discouraged. Tumors which are often demonstrably not encapsulated (Fig. 8, Case 34), which frequently recur after bronchoscopic removal (Cases 2, 5, 15, 32, 33, 34), which may infiltrate surrounding tissues (Fig. 9, Case 1; Fig. 10, Case 37), and which frequently (Cases 23, 24, 25, 26, 30, 31, 32, 33, 38) metastasize, are far from benign. The truth is that here, as with other similar kinds of neoplasms, "benign" and "malignant" are only relative terms, and all gradations of behavior, as well as of their structure, are to be seen between highly differentiated, more slowly growing adenomas (Case 1, I.K.) and poorly differentiated infiltrating and

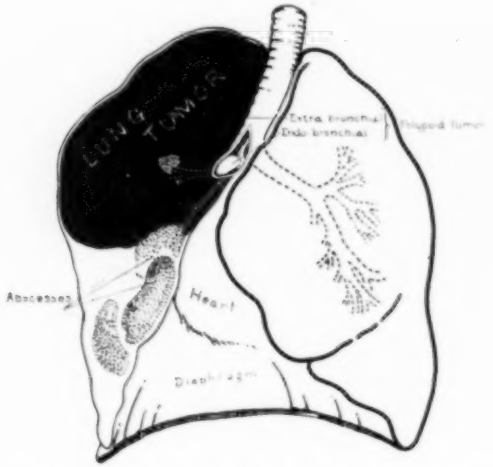


FIGURE 9. Case 1: I.K. Artist's diagram from postmortem specimen. Large adenomatous bronchial tumor, carcinoid type, obstructing right stem bronchus, untreated. Death from brain abscess. Duration 20 years. Note impossibility of bronchoscopic removal. Same case as Figure 12.

metastazing carcinomas (Case 33, E.S.). In the case of these adenomatous neoplasms, most of the tumors occupy an intermediate or borderline position in the scale of behavior often designated as potentially Graham[77] or semi-malignant Ackerman.[78] The prognostic question here should not be, "Is this tumor benign or malignant?" but "How benign, or malignant, is this particular tumor likely to be?" At the present time we liken their malignancy to that of gastrointestinal carcinoids, parotid mixed tumors, "benign" basal cell epithelioma, sweat gland tumors of the skin, thyroid "benign" metastasizing carcinomata, "benign" rectal and bowel polyps. This degree of malignancy is such as to warrant early lobectomy or pneumonectomy or at least complete surgical resection (bronchotomy) when the former is not feasible (23 of 38 cases).

Do such relatively benign tumors become malignant, and do recurrences show enhanced malignancy? McFarland[79] and Patey[80] for mixed tumors of the parotid answered this question in the negative; and concluded that while different tumors show different degrees of malignancy, a single tumor shows little or no change of structure or rate of growth in its recurrences. This is

FIGURE 10. Case 37: J.R. Adenomatous bronchial tumor, carcinoid type. Surgical specimen of removed right lower and right middle lobes showing section through tumor and abscess in right lower lobe. Note impossibility of bronchoscopic removal and the tumor infiltrating toward the sectioned trabeculated abscess wall. Duration 6 years ;alive and well one year, multiple lobectomy and 16 months after surgical drainage of right lower lobe abscess and empyema. Same case as Figures 16 and 17.

also probably true of the majority of adenomatous bronchial tumors. Thus in most patients with distant metastases there was a long history of known bronchial tumor but no exceptional transformation of growth appeared (Case 31, S.N.M.). But it seems likely that distant metastases are more an accident of lymphatic and blood vessel invasion and that the metastatic liver and bone disease is accounted for in this way. However there are rare exceptions to this such as Case 33, E.S., in which the histological examinations over a 6 year period showed a marked change from a pattern without detectable pleomorphism or carcinomatous change to one with anaplasia and pleomorphism and carcinomatous structures. The rate of growth showed a marked acceleration as evidenced by bronchial wall infiltration bronchoscopically and asphyxial symptoms terminating in death and autopsy. A similar instance occurred in Case 32, A.H. Both of these cases were tumors of the carinal area and of the so-called "cylindromatous" or "mixed tumor" pattern (Figs. 5 and 5A). Those with carcinoid patterns have not

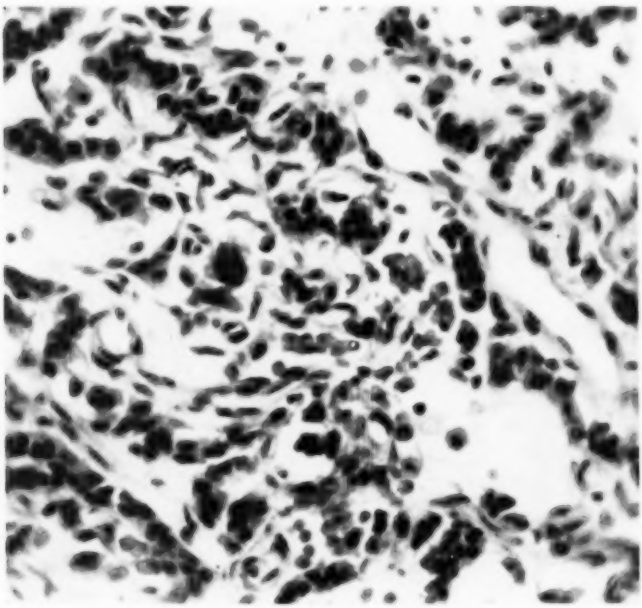


FIGURE 11. Case 2: J.B. Symptoms 12 years, when this tumor removed bronchoscopically in 1928; microscopic section of original biopsy carcinoid type. Patient, a woman now 56. Diagnosed carcinoma in 1928. Radiation therapy. Now (1950) patient has a regrowth with cystic bronchiectasis of the obstructed right lung. Is invalided because of hemoptysis and pulmonary suppuration .now 35 years since onset of symptoms.

yet been observed by us to undergo this kind of transformation although as indicated they did reach a large, local size and metastasized regionally and distantly after long duration but with no marked change of histological pattern.

The following detailed case history illustrates the classical clinical manifestations such as onset with asthmatoid symptoms, followed by pulmonary hemorrhages and suppuration which led to the suspected diagnosis of both asthma and tuberculosis. In addition there was the usual fatal prognosis given her by misinterpreting the bronchoscopic biopsy as bronchogenic carcinoma. Then bronchoscopic removal and radiation therapy, the usual treatment prescribed in the thirties, which has now been supplanted by pulmonary resection, was followed after twelve years by a complete recurrence with a destruction of the entire left lung without demonstrable distant metastases. The overall duration of symptoms is twenty-eight years and it is twenty-two years since bronchoscopic removal. Today, early pulmonary resection would have

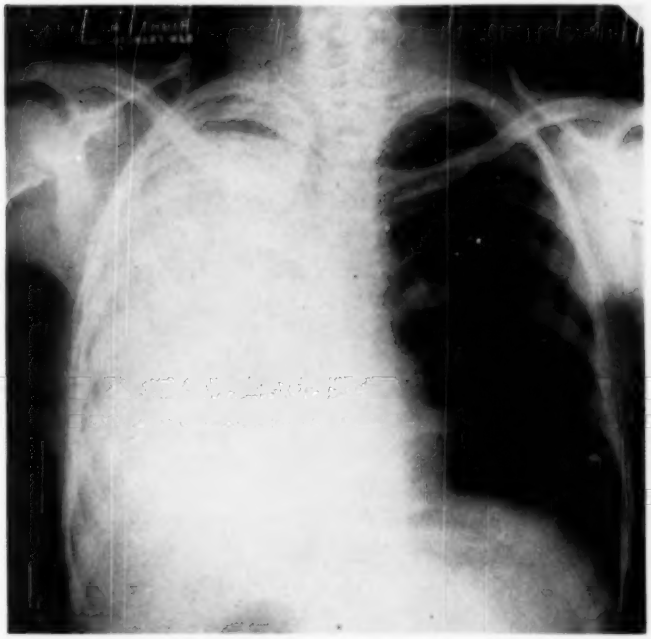


FIGURE 12. Case 1: I.K. X-ray film of chest January 4, 1921 showing empyema obscuring underlying tumor mass and destroyed right lung. Expired October 27, 1937 of brain abscess, duration 20 years. Carcinoid type adenomatous bronchial tumor. Same case as Figure 9.

obviated the quarter century long period of disability and the present threat of distant metastatic disease (See Cases 23, 25, 26, 27, 30, 32, 34, 35, 36, 37).

Case 2: J.B., aged 47, was first admitted to the University of California Hospital on March 8, 1928.

The onset occurred with cough, colds, and choked up sensations beginning in 1915 shortly following confinement. Soon afterward she noted wheezing localized to the upper right chest, which was brought on by exertion.

She was fairly well until 1922. At this time her wheezing and asthmatoid symptoms increased. Her husband died of pulmonary tuberculosis that year, and, until 1928, she was suspected of having tuberculosis. Hysterectomy was performed in 1923 for uterine fibroids, and following this she had some increase of her periodic asthmatoid symptoms. In 1926 her cough became more productive, and she had four pulmonary hemorrhages, with more than one cupful on two occasions. A diagnosis of pulmonary tuberculosis was made by her family doctor, who after pulmonary x-ray examination in 1928 made a presumptive diagnosis of cancer of the lung. Bronchoscopic examination on March 8, 1928 dis-

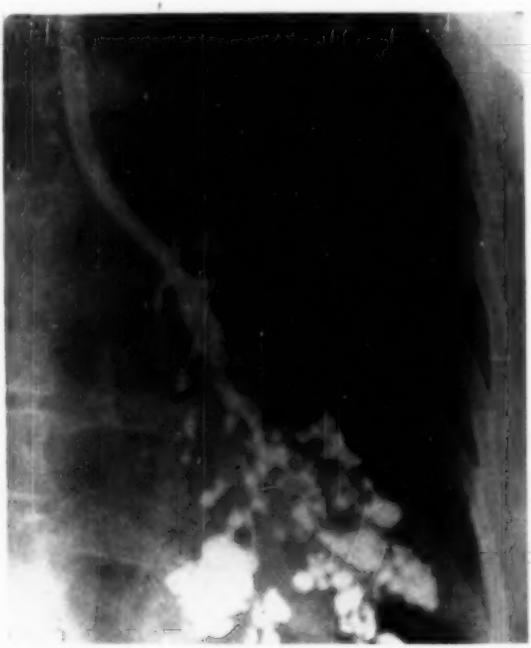


FIGURE 13. Case 10: F.J. November 3, 1938 serial selective bronchogram with lipiodol. Spot film showing cystic bronchiectasis limited to two segments of left lower lobe. Living and well, total duration 18 years, 10½ years after left lower lobectomy. Same case as Figure 14.

closed a large, firm polypoid tumor in the right stem bronchus. The entire presenting portion of the tumor was removed. Histological diagnosis of the bronchoscopic material was carcinoma (Fig. 11, Case 2, J.B.), later changed to adenomatous bronchial tumor, carcinoid type.

Shortly after the bronchoscopic removal of the tumor, she developed a severe pulmonary infection. X-ray therapy was instituted for several months and improvement followed.

She worked as a waitress throughout the following years, usually in very good health without dyspnea. There were recurring pulmonary infections, however, almost yearly from 1930 to 1935. During this time she was troubled with an annoying cough and considerable expectoration, and resorted to postural drainage. In 1935 she was given an autogenous vaccine, with marked improvement in cough and sputum so that she was much relieved until December 1937. Then alarming hemorrhages with pulmonary infection recurred. For these she was hospitalized in December 1937; June 1939; October 1939; and January 1940. The last necessi-

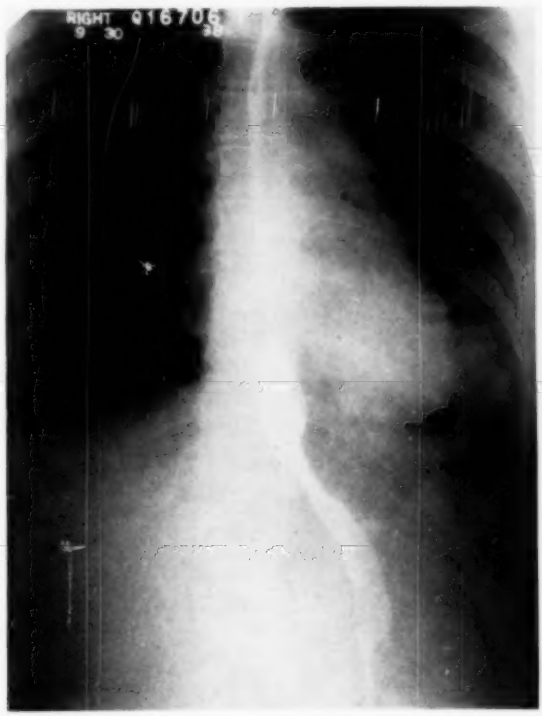


FIGURE 14. Case 10: F.J. X-ray film of chest September 30, 1938 showing left lower lobe partial atelectasis due to carcinoid type of adenomatous bronchial tumor obstructing two segments of the left lower lobe. Duration 18 years, alive and well 10½ years after left lower lobectomy. Same case as Figure 13.

tated a stay of three weeks. Excitement and exertion brought on hemorrhages.

She was not observed at the University of California Hospital from 1928 until February 1940. At this time she re-entered for study, having just recovered from her attack of "pneumonia" that had begun 3 weeks before.

On entry the patient noticed she was unable to lie on the affected (right) side. Voluntary pressure to the right chest wall with her hands produced soft, semi-solid sputum and brought relief of the dyspnea and feeling of fullness in the right chest. At times extension of the right

FIGURE 15. Case 12: G.D. Artist's drawing of surgically resected left lower lobe. Adenomatous bronchial tumor, mixed tumor type. Duration 20 years; alive and well 9½ years after lobectomy. (Top) Section of tumor 7.0 cm. in diameter. Note shrunken abscessed and bronchiectatic lobe. (Bottom) External appearance showing numerous pleural adhesions. Same case as Figures 4 and 7.

shoulder facilitates the raising of sputum, and she became conscious of the entrance of air into the lung after it had been emptied. She had a marked postural and wheezing dyspnea when she lay on the affected side, which caused her to sleep on her left, or good side. (This is unusual since most patients with such bronchial obstruction favor the side of the obstructed lung).

Physical examination revealed a healthy, robust individual. She was without fever. There were signs of atelectasis of the right lung, with displacement of the mediastinum to the right. A marked inspiratory and expiratory wheeze could be heard over the right chest, which diminished or became absent when the patient lay on the left side.

Plain x-ray films taken February 15, 1940 disclosed a shrunken right lung with displacement of the heart and trachea into the right chest, and numerous whorls typical of cystic disease occupying the remains of the right lung. No definite tumor could be seen in the plain x-ray films taken in different views and densities.

Tomographic studies made on February 4, 1940, at 8 centimeters from the back depict the outline of the displaced trachea, the carina, and the right stem bronchus. Almost filling the right stem bronchus is distinctly seen an endobronchial tumor with larger extrabronchial lobular exten-

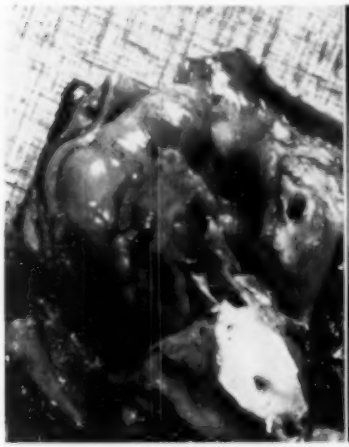


FIGURE 16

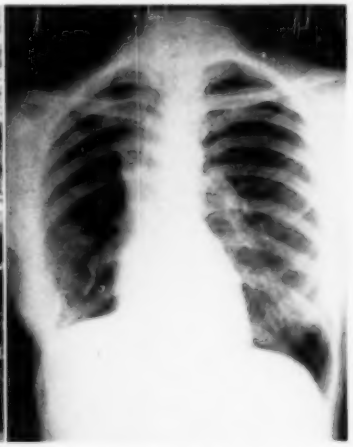


FIGURE 17

Figure 16. Case 37: J.R. Adenomatous bronchial tumor, carcinoid type, right intermediate bronchus. Surgical specimen of removed right middle and right lower lobes showing sessile attachment, complete obstruction to right lower and partial obstruction to right middle lobe. Duration 6 years; living and well one year after multiple lobectomy and 16 months after surgical drainage of right lower lobe abscess an dempyema. Same case as Figures 10 and 17.

Figure 17. Case 37: J.R. X-ray film of chest April 1, 1950, 12 months after multiple lobectomy right lower and middle lobes for adenomatous bronchial tumor, carcinoid type, of the right intermediate bronchus. Lobectomy preceded by thoracotomy, rib resection and drainage of empyema and abscess in right lower lobe. Note expansion of right upper lobe. Duration 6 years; alive and well one year postoperatively. Same case as Figures 10 and 16.

sions. In the lateral view, the endobronchial portion is well seen at a depth of 11 centimeters from the right side of the chest.

Bronchoscopy was again performed on March 13, 1940. This disclosed a pinkish, soft, round polypoid tumor in the right stem bronchus almost completely obstructing it. The tumor extended to the level of the tip of the carina and was attached to the lateral side of the right stem bronchus. No secretions were seen although the suction tube could be passed along the mesial bronchial wall for a distance of 1 centimeter from the tip of the tumor. The bronchial tree was remarkably free from secretions, and normal in color. Bleeding was not produced. The patient refused to have a biopsy taken at this time.

Subsequently a second bronchoscopy and biopsy disclosed no change in the histological carcinoid pattern. Since 1940 she has remained invalided from hemorrhages and bouts of fever. She is alive now approximately 35 years since onset of symptoms without demonstrable metastasis, although one suspects regional node metastases.

From the point of view of clinical course, this tumor is benign. It is still present in the bronchus and has continued to grow in spite of the fact that all the visible bronchoscopic tumor was removed 22 years ago. Unquestionably it has now reached a large size but has not shown evidence of distant metastases. We believe this tumor has potentially the power to invade pulmonary vessels and to metastasize in different places, such as mediastinum, bones and liver.

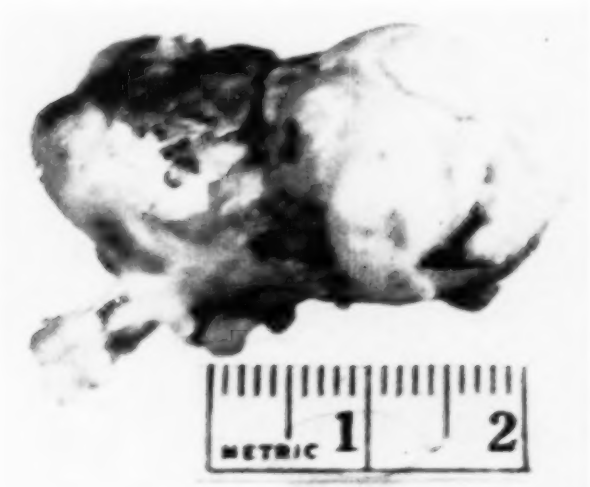


FIGURE 18. Case 35: A.P. Early adenomatous bronchial tumor, clear cell, glandular type. Surgical specimen removed through left transpleural bronchotomy from left carinal area. Note pedicle with mucosa attached. Alive and well one year after bronchotomy with clear left lung. Total duration 2 years, left lung clear. Same case as Figure 6.

The next case history illustrates more dramatically the cause of death associated with the serious and severe pulmonary suppuration (Figs. 10, 12, 13, 14) resulting from the bronchial obstruction caused by polypoid adenomatous tumors obstructing the bronchi, whereas in the previous case 2, J.B., suppuration was mild. In this case 5, I.W., suppuration led to brain abscess and death.

Case 5: I.W. This is a case of a man who was about 46 when symptoms started, and 52 when he died of a brain abscess and suppuration of the left lung. He entered the University of California Service of the San Francisco Hospital complaining of cough, expectoration, and chest pain. His illness began in 1926 when he started to have fever, anorexia, and a productive cough, raising large amounts of foul pus. He developed severe joint pains and headaches, and finally went to Arizona. While there all symptoms became worse so he went to Los Angeles where bronchoscopic examination was finally done and a tumor mass found obstructing the left main bronchus. He was bronchoscoped two or three times a month, so that up to the present he has had 50 bronchoscopies. At various times

FIGURE 19. Case 35: A.P. Cross section x 2 of adenomatous bronchial tumor, clear cell, glandular type removed from left subcarinal area by posterior transpleural bronchotomy. Bulk of tumor appeared to be serous secreting glandular epithelium. Total duration 2 years; alive and well one year after bronchotomy, left lung clear. Note the large cystic spaces. This is similar to clear cell papillary cystadenoma of salivary glands (Bauer). Same case as Figures 6 and 18.

some of the tumor mass was bitten away and radium implanted. His condition, in general, improved.

Physical examination: Male of about stated age, generally undernourished and dyspneic. Signs of shrunken atelectatic obstructed left lung were elicited.

Bronchoscopy showed benign tumor arising from left main bronchus extending across carina. On coughing the right bronchial wall so approximated the tumor that there was practically no air passage. Radium seeds were implanted. This was complicated by empyema and bronchopleural fistula which was treated by rib resection and drainage at the University of California Hospital.

On February 6, 1930, he re-entered San Francisco Hospital. Physical signs were unchanged except that breath and voice sounds were absent on the left, posteriorly. Bronchoscopy showed the same findings as before except that pus could be seen spilling around the tumor mass, coming from the left main bronchus.

On the third entry at the San Francisco Hospital, March 28 to April 17, 1930, the patient had been improving since last entry but two days previously he suddenly developed a terrific headache, fever, cough, bloody sputum, left chest pain, and a choking sensation when lying on right side. Since previous discharge the tumor mass was fulgurated and up to this entry the patient had had about 75 bronchoscopies in all.

Examination showed him to be more toxic, markedly dyspneic, lying on side, raising thick, tenacious, greenish, blood-stained sputum. Slight

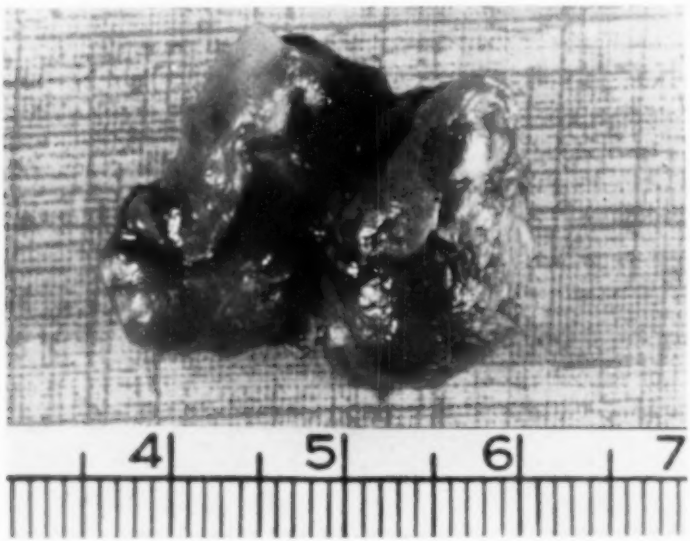


FIGURE 20. Case 34: S.S. Adenomatous bronchial tumor, carcinoid type, recurrent following bronchoscopic removal seven years before bronchotomy. Surgical specimen removed via transpleural bronchotomy, sessile attachment to right subcarinal area. Duration 8 years; alive and well 4 months postoperatively with clear right lung. Same case as Figures 8 and 21.

movement of patient caused proxysmal coughing. Pulse rate, 120. Chest findings essentially the same as before. X-ray film now showed trachea displaced to the left, with left hydrothorax. Laboratory findings: Urine, negative; Blood, Hgb. 90 per cent; RBC 4,250,000; WBC 12,960; PMN 80 per cent; S.L. 9 per cent; L.L. 4 per cent; Transitional cells 7 per cent. Blood Wasserman: Negative. Patient was given thoracotomy drainage and sedatives. Discharged from hospital 3 weeks after entry unimproved.

On the fourth entry at the San Francisco Hospital, December 18 to 22, 1931, patient had had a left thoracotomy since last entry, when lung abscess was drained at the University of California Hospital. During the past 4 months he had gradually developed a right-sided hemiplegia and atypical aphasia.

Examination showed the patient in extremis, unable to move the right side of his body, with a thoracotomy wound in left chest which was draining a small amount of purulent material.

Examination of chest essentially as before. There was paralysis of right 7th, 12th cranial nerves. Diminished motor power of right arm and lower limb with hypertonicity and muscle spasm over right side of body. Deep reflexes hyperactive on right side. Abdominals absent. Has atypical motor aphasia. He was extremely weak and the course was rapidly progressive. He expired four days after entry, six years and four months after his

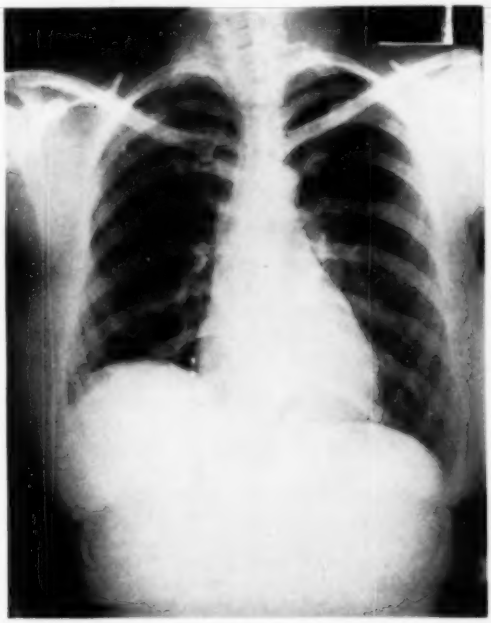


FIGURE 21. Case 34: S.S. X-ray film of the chest, April 10, 1950, 4 months after right transpleural bronchotomy. Preoperative complete atelectasis of the right lung cleared within a few days after surgery. Note the well aerated right lung. Same case as Figures 8 and 20 .

illness began. The necropsy was started one and one-half hours after death. The important findings were in the chest and brain, which are abstracted from the complete report.

There were two scars in the left axilla. One was healed and paralleled the 4th interspace in the region of the anterior axillary line. The other one was about the level of the 5th interspace in the posterior axillary line and showed a slight chronic drainage. Both were about 8 cm. in length. There was clubbing of the fingers of both hands.

The left diaphragm extended up to the 5th rib, right diaphragm to the 4th interspace. The mediastinum and contents were pulled far over into the left chest. The left lung could not be seen with the organs in situ. The right lung was tremendously hypertrophied and extended well into the left chest. Right pleural cavity was negative.

The right lung was tremendously hypertrophied and weighed 940 grams. On external examination all the lobes were enlarged and edematous. On the lateral aspect of the lower lobe there was a peculiar area of calcification with parallel spicules of calcification, somewhat like the prongs of a rake, measuring about 3 cm. in length and about 1 mm. in diameter. There were no adhesions over this area. On cut sections there was found a small cavity enclosed by these calcified spicules but containing no fibrous tissue. The spicules seemed to outline the interlobular connective tissue. Cut section of the entire lung showed a very marked edema and congestion with fluid pouring from the cut surface. There was a small amount of pus in some of the larger bronchi.

The left lung was markedly decreased in size and lay, a small mass, behind the heart along the left side of the vertebral column. It was firmly bound down by adhesions. On removal it was found to be an atelectatic mass measuring 12 x 8 x 5 cms. The mass was firm and fibrotic and except for the bronchi had no resemblance to lung tissue. It was reddish in color and covered by a greatly thickened pleura. On cut section it was found to be fibrous tissue with a few dilated bronchi in its substance. On removing the lung, old cavities containing a small amount of hemorrhagic pus were broken into, lying in the adhesions about the lung.

Two cm. below the bifurcation of the trachea in the left main bronchus, there was a large tumor on a pedicle measuring about 3 cm. in diameter, the pedicle measuring 2 mm. in diameter and being about 2 cm. long. The tumor hung down in the bronchus and could be moved about with ease on the pedicle. On cut section there was calcification in the core of the tumor. About 2 cm. below this there was another similar papillomatous structure also on a pedicle, extending down into the bronchus of the lower lobe of the left lung. This second tumor had two pedicles attached next to each other to the bronchial wall. The bronchi distal to these tumors were inflamed and contained mucopurulent exudate. There was no functioning lung tissue on this side. The hilar lymph nodes on both sides, more marked on the left, were markedly enlarged and edematous. The trachea and bronchi were pulled sharply over into the left chest by the chronic adhesions.

Brain: There was free pus about the base of the brain. On external palpation, the left frontal lobe was much softer than normal. Cultures and smears of the pus were taken which later grew out of an anerobic, partly hemolytic, streptococcus.

The brain showed shallow sulci and flattened convolutions. On verticle

section the right lateral ventricle was larger than the left. The left lateral ventricle contained pus. There was an abscess in the white matter of the left frontal lobe, the diameter of which varied from 6 to 10 mm. The abscess was 3.5 cm. in length and in its middle had a small pocket extending laterally and measuring 1 cm. in diameter. It contained a greenish-yellow pus. There was also a tiny hemorrhage, 1.5 mm. in diameter, in the center of the left thalamus.

Microscopic examination: Microscopic examination of the left lung showed a practically complete fibrosis containing lymphocytes and carbon particles. The few remaining alveoli were nonfunctioning and their epithelium was cuboidal in type resembling glands. The bronchi showed extensive chronic infiltration of their walls with large bronchiectatic dilatations and accumulations of pus in their cavities. There was no evidence of tuberculosis. Sections through the bronchial tumor showed a fibrocartilagenous core with a pseudostratified epithelium covering it. Sections were not taken from the calcified portions. Sections through the bronchial nodes showed anthracosis and an endothelial hyperphasia with fibrosis of the germinal centers.

Sections through the right lung showed emphysema, congestion and some edema with scattered peribronchial areas of pneumonia exhibiting red blood cells, desquamated epithelium, polymorphonuclears, serum and practically no fibrin.

Sections from the brain showed a pus filled abscess cavity surrounded by a rather thick wall of glial proliferation. The adjacent brain tissue was edematous. Sections through the lateral ventricle showed pus in this cavity. The left thalamus had recent hemorrhage with a few pigment filled macrophages.

The final diagnoses were: Calcified adenomas of the left bronchus with atelectasis and fibrosis of the left lung and bronchiectasis and abscess formation. Chronic, fibrous obliteration of the left pleural cavity with displacement of the mediastinum into the left chest. Metastatic brain abscess, left side. Compensatory emphysema and edema of the right lung. Localized calcification of the right lower lobe (true ossification). Chronic cholecystitis and cholelithiasis with a stone in the cystic duct.

In contrast to the preceding case are such cases as 12, G.D., Figs. 4, 7, 15 and Case 37, Figs. 10, 16, 17. The difference in time required to obtain a cure and removal of this tumor although the suppurative disease was just as serious, and the prevention of a fatal outcome due to the pulmonary suppuration by early surgical intervention are illustrated by case 37. Less than six months intervened between the time of diagnosis and time of pulmonary resection. The satisfactory end result in case 37 treated with pulmonary resection compared to the death resulting in case 5 which was treated bronchoscopically speaks for itself. Modern antibiotics and antibacterial drugs were utilized in association with pulmonary resection to manage this serious suppurative disease as well as the adenomatous bronchial tumor in this case.

Case 37. J.R., white female, aged 40 years. Onset of symptoms in 1944; wheezing, hemoptysis and frequent winter colds. These symptoms were not disabling until 4 years later when she had a serious episode of pneu-

monia associated with right pleurisy. Convalescence was slow and was accompanied by cough and bloody, foul sputum. She was able to continue working after this for several months but hemorrhages became more severe from time to time and therefore she was finally referred for examination and treatment and entered Cedars of Lebanon Hospital November 19, 1948.

Physical examination at that time showed she was well nourished. There was a male type of habitus with small breast, male escutcheon, and marked clubbing of the fingers. Examination of the chest disclosed dullness, diminished breath sounds and rales over the right base. X-ray films and fluoroscopy of the chest showed a dense cloudiness throughout the lower two thirds of the right lung. There was a mediastinal shift on fluoroscopic examination to the right side. Sputum became very copious and foul and fever ranged from 101 to 103 degrees F. She was given antibiotics and sulfa drugs.

On November 20, 1948, bronchoscopy was done which disclosed a tumor in the right intermediate bronchus projecting above the level of the lower border of the right upper lobe and obstructing both the middle and lower lobes. It had a broad attachment to the medial posterior wall of the bronchus, was bosselated, reddish pink, and covered with some exudate. Biopsy of this tumor was taken which showed numerous compact clumps of cells separated by fairly dense fibrous septa. The cells were small, spherical, uniform in appearance with small dark nuclei and scattered chromatin. Diagnosis of the biopsy was adenomatous bronchial tumor.

It was obvious that she had had a serious pulmonary suppuration for some time and that the bronchial adenoma was interfering with drainage. It was, therefore, decided to perform a drainage of the pulmonary abscess first and when this suppurative disease had subsided to proceed with pulmonary resection, removing both the diseased lung and the tumor in one sitting. So on November 23 a thoracotomy and rib resection were performed with drainage of interlobar empyema and abscess of the right lower lobe. The wound was packed with penicillin and streptomycin soaked gauze. After one week she was allowed to go home and returned for dressings and examinations. When the drainage had practically ceased and the chest wall sinus was very small, she re-entered Cedars of Lebanon Hospital on April 29, 1949 and on May 3 multiple lobectomy with removal of the right middle and lower lobes was performed. At htis time the sinus in the chest wall was closed. There was found in addition to the tumor, enlarged bronchial artery, obliterated interlobar fissure of dense scarring between the middle and lower lobes and a large abscess within the lower lobe (Fig. 10) and although during dissection some of the lung was torn, her postoperative course was quite satisfactory, no empyema developed.

Bronchoscopy postoperatively disclosed satisfactory healing of the intermediate bronchus and no evidence of recurrence. The surgical specimen (Figs. 10, 16) showed an adenomatous bronchial tumor of the carcinoid type as well as the bronchopulmonary cutaneous fistula communicating with the abscess cavity in the apex of the lower lobe. In the lower part of the lower lobe an irregular, ragged, hour-glass cavity 4 x 2 cm. which showed some bloody mucus was encountered. A sausage shaped, gray-tan ovoid tumor mass 3 x 1.5 cm. completely blocked the superior segmental branch of the lower lobe and middle lobe (Fig. 16). On section the tumor mass extended in a rather smoothly demarcated

fashion into the underlying distorted parenchyma (Fig. 10). Sections through the mass showed a neoplasm made up of islands of fairly uniform cells having an oval nucleus with a darkly staining coarse chromatin structure. There was a small amount of cytoplasm. In some places the tumor islands were separated by a small amount of fibrous connective tissue stroma and in a few places the tumor formed gland-like spaces. In one area there was infiltration throughout the bronchial wall and the mucosa was replaced by tumor extending beyond the cartilage, and in other areas mucus-secreting glands have been invaded. The lung still showed a tremendous fibrosis with acute and chronic inflammation, marked bronchiectasis and in one area a very marked squamous metaplasia. In one area, a granulomatous mass projected into the lumen. There was tremendous fibrous thickening of the pleura.

The patient was discharged from the hospital on the tenth postoperative day and one month later returned to work as a clerk.

On followup visit, March 18, 1950, 11 months postoperative, patient complained of slight cough at times, but was working regularly as a clerk. X-ray and fluoroscopy of the chest on April 1, 1950 showed satisfactory re-expansion of the upper lobe, no evidence of recurrence and satisfactory mobility of the right diaphragm (Fig. 17, J.R.).

This case also illustrates the different management of adenoma compared to carcinoma of the lung where the time element is far more important. Preparation for lobectomy or pneumonectomy requiring several months does not interfere with a satisfactory final result. The patient with usual bronchogenic carcinoma cannot afford this much time else metastases are apt to supervene.[81]

Case 35: A.P. A variant of adenoma, which we prefer to designate as a clear cell, glandular type, has been uncovered. This young girl of 14 years had onset with the usual wheezing, followed by symptoms of pneumonitis and hemorrhages. The tumor was located in the left stem bronchus, very high up, attached by a narrow pedicle to the medial wall of the left stem bronchus just one quarter inch below the carina. Symptoms were only of six months' duration at the time she was admitted to the Los Angeles County General Hospital, Torrance Branch. X-ray films of the chest showed a complete atelectasis of the left lung. Temperature was 100 to 101 degrees F. Bronchoscopic examination disclosed a polypoid tumor mass obstructing the left stem bronchus. It was slightly mobile and mucus exuded around it.

It was realized that because of the nearness to the carina, pulmonary resection would have to include the entire left lung and a portion of the carina in order to get above the tumor. Therefore it was decided to perform an exploratory thoracotomy and if possible to remove the tumor through a left stem bronchotomy. This operation of transpleural bronchotomy was performed on April 20, 1949. The left stem bronchus was dilated at its origin from the trachea. The tumor could be felt through the soft wall of the bronchus. The entire left lung was atelectatic. There were no adhesions. The bronchus was opened just distal to the tracheal bifurcation for a distance of 2 cm. When this was done, approximately 25 cc. of clear mucoid fluid was aspirated from the left stem bronchus distal to the tumor. The tumor itself was bosselated, approximately 4 cm. in length and 3 cm. in width. It had a stalk attachment to the medial

wall of the left stem bronchus, one-half cm. from the tip of the carina and the stalk itself was about 1 cm. in length and one-half cm. in width, base only 3 mm. in diameter at the attachment to the mucosa (Fig. 18, Case 35, A.P.). When the bronchus was incised, the tumor prolapsed through the incision and it was easy to see the point of attachment. Following section of the stalk at the mucosa the point of attachment was carefully fulgurated with high frequency cautery. The bronchus was then closed with interrupted fine silk. Following closure of the bronchus the left lung expanded completely. Examination of the specimen disclosed a polypoid tumor with necrotic areas on the surface, the surface bosselated and of the size previously mentioned. The microscopic sections did not have the picture of any of the usual adenomata of the bronchus. They showed columnar mucus producing cells not commonly found in the carcinoid type. Specimen was sent to Dr. Paul Klemperer who found definite cilia in some of the surface cells and he felt the tumor probably arose from bronchial epithelium. Pathologist of Harbor General Hospital, Dr. Ellen P. Feder, and pathologist of the Washington Medical School, Dr. Robert A. Moore, both agreed that it was not the usual variety of bronchial adenoma (Figs. 16, 18, 19). Therefore this tumor composed of mucous producing cells is currently being classified as an adenomatous bronchial tumor of clear cell, glandular type because it seems probable that it arose from the serous mucous glands. Serial microscopic sections of the mucosal end of the stalk and the bits of bronchial tissue removed from the site of attachment showed some stellate cells but no glandular epithelial cells, indicating all the tumor had been eradicated or removed.

Followup 11 months after bronchotomy disclosed that she attends high school regularly, suffers from no sputum or cough, and that x-ray films of the chest show a well aerated left lung.

Another variant which has come to our notice was recently reported by Kraus et al.[41] as a myoblastoma of the bronchus which Dr. Evarts Graham[77] felt represented a variant of adenomatous bronchial tumors. Little has been written of the myoepithelium of the bronchial glands as a possible tissue origin producing bronchial tumors. Sheldon[82] however has stated that the contractile epithelial cell may be found in mammary, eccrine, apocrine, Moll's glands of the eyelid, cerumen glands of the ear and the salivary and lacrimal glands. Hamperl[83] felt that epithelium or transition from myoepithelium produced reticulum, collagen, mucus, cartilage, and ground substance. Myoepithelium of the bronchial tree does not yet appear to have been given sufficient study. One wonders whether the two tumors just mentioned, namely Case 35 and the myoblastoma reported by Kraus could have arisen from this type of tissue associated with the bronchial mucous glands. Willis[84] states that the term myoblastoma should be dropped altogether although it would appear that the myoepithelium of bronchial glands logically would play a role in the production of the stromal elements especially the hyaline portions, while the parenchymal tumor mass is from proliferation of glandular or ductal epithelium. In this connection Lever[85] has brought out in discussing benign

tumors of the cutaneous appendages and basal cell epitheliomas that the pathogenesis of sweat gland cylindroma is concerned with the proliferation of cells with round or elongated small dark staining nuclei arranged in palisade formation at the periphery of the epithelial cell masses, regarded as cells differentiating toward myoepithelial cells of apocrine glands. Furthermore he has shown that some myothelial sweat gland tumors possess a considerable amount of stroma with hyaline appearance and areas of mucoid or cartilaginous transformation. As with the adenomatous bronchial tumors, these tumors of skin exhibit transitions from one type of variant to another thus they merge from sebaceous nevus to sebaceous adenoma, to sebaceous epithelioma, to cystic basal cell epithelioma. Certain of our cases seem to behave as these skin tumors do. Thus cases 32, A.H. and 33, E.S. instead of mixed tumor or cylindroma might be called cystic basal cell epithelioma. However it would appear less confusing until more information is available to continue using the term adenomatous bronchial tumor, adding carcinoid, mixed tumor, cylindromatous, myoepithelial or clear cell glandular type, as the case may be, recognizing that these terms are probably still not completely descriptive of the entire pathogenesis of these tumors. At the same time we should recognize tumors exhibiting a frank malignant change as carcinoma.

The fourth and most malignant type of adenomatous bronchial tumor, mixed and/or cylindromatous type, has exhibited frank malignant tumor, in two cases, 32 and 33, with numerous metastases at postmortem.[21] Both were treated by bronchoscopic removal plus radiation. Each was located in the stem bronchi close to the lower end of the trachea and asphyxial symptoms resulted. Biopsies early in the clinical course suggested usual bronchial adenoma but within six years death resulted. Postmortem examinations disclosed the metastases of frank adenocarcinoma in each case. In addition to our own observations the literature now contains a fair number of references to patients with adenomatous bronchial tumors and proven distant metastases beyond the thorax to liver and bone; besides in at least three instances,[36,22,31,13] these metastases have been stated to be the cause of death.

When we have separated the distinctive group of adenomatous bronchial tumors, there is left a rather miscellaneous assortment of rare, benign, bronchial and pulmonary tumors, papillomas, fibroadenomas, fibromas, hamartoma, chondromas, lipomas, angiomas, and inflammatory polyps. In our experience these tumors form less than 5 per cent of the so-called benign bronchial or pulmonary tumors. Usually these tumors do not reach a large size because most of their symptomatology arises by virtue of the

fact that they are located within the bronchial tree, although occasionally a peripheral tumor of the larger size has been reported. Their importance clinically has been very minor.

Diagnosis rests upon the microscopic interpretation of either bronchoscopic biopsy or the surgically resected specimen. Treatment may be bronchoscopic to reestablish the bronchial airway and drainage, but bronchotomy or pulmonary resection may be indicated either for the tumor or to eradicate the accompanying pulmonary suppuration.

SUMMARY AND CONCLUSIONS

1) Thirty-eight cases of adenomatous bronchial tumors are briefly reported.

2) So-called benign tumors of the lung and bronchi are most frequently adenomatous bronchial tumors.

3) Adenomatous bronchial tumors are a group of several histologic variants, the most common of which are the carcinoid, mixed tumor and cylindromatous types. Glandular and myoepithelial types occur.

4) These tumors are extremely important because on the one hand they represent potential malignant tumors and on the other clinically curable tumors.

5) They produce symptoms and often death largely through pulmonary suppuration resulting from bronchial obstruction but also they are prone to serious hemorrhages. They may after many years metastasize and even produce death associated with metastases.

6) Bronchoscopy is always indicated for biopsy of the tumor and in approximately 90 per cent the tumor is accessible to bronchoscopic biopsy because of its location in a lobar or stem bronchus.

7) The ideal treatment is removal of the tumor with lobectomy or pneumonectomy. Twenty-three of the 38 patients in this series had surgical resection therapy: 21 were lobectomy or pneumonectomy; two were resected via transpleural bronchotomy (Case 35, Figs. 6, 18, 19 and Case 34, Figs. 8, 20, 21); one had lobectomy plus bronchotomy (Case 15, A.B.); and one had plastic bronchotomy only (Case 33, E.S.).

8) The remainder of the benign bronchial and pulmonary tumors occur infrequently and represent a clinically unimportant group but like all polypoid tumors of the bronchi even though of small size they may produce serious clinical manifestations.

RESUMEN Y CONCLUSIONES

1) Se refieren treinta y ocho casos de tumores bronquiales adenomatosos.

2) Los tumores llamados benignos del pulmón y de los bronquios son los más frecuentemente tumores bronquiales adenomatosos.

3) Los tumores adenomatosos bronquiales constituyen un grupo con diversas variantes histológicas. Las más comunes de ellas son: el carcinoide, tumores mixtos y tipos cilindromatosos. Los tumores glandulares y los mioepiteliales pueden ocurrir.

4) Estos tumores son extremadamente importantes, porque en primer lugar representan tumores potencialmente malignos y en segundo son clínicamente curables.

5) Ellos producen síntomas y a menudo la muerte a consecuencia de supuración resultante de obstrucción bronquial, pero también son capaces de producir hemorragias serias. Pueden después de muchos años metastatizar y aún producir la muerte con metástasis asociadas.

6) La broncoscopia es siempre indicada para biopsia del tumor y en aproximadamente 90 por ciento de los casos el tumor es accesible por su ubicación en un bronquio lobar o principal.

7) El tratamiento ideal es la lobectomía o la neumonectomía. Veintitrés de los 38 enfermos de esta serie sufrieron resección. Veintiuno fueron lobectomías o neumonectomías. Dos fueron resecados por la vía de broncotomía transpleural (Caso 35, Figs. 18, 19 y Caso 34, Figs. 8, 20, 21). Uno se sujetó a lobectomía más broncotomía (Caso 15, A.B.) y uno tuvo broncotomía plástica solamente (Caso 33, E.S.).

8) El resto de los tumores benignos pulmonares y bronquiales ocurren con poca frecuencia y representan un grupo de poca importancia clínica pero como todos los tumores polipoides de los bronquios aún los de pequeño tamaño, pueden producir manifestaciones clínicas serias.

TABLE OF CASES

Ages Given at Onset of Disease

Case 1: I.K., (U.C.H.) white female, aged 28, carcinoid pattern, endo-extrabronchial, 13.5 cm. in diameter, right stem bronchus and right upper lobe, empyema, surgical drainage with persistent sinus until death. Duration 20 years; postmortem: death from brain abscess and pulmonary suppuration, no metastases (Figs. 9 and 12).

Case 2: J.B., (U.C.H.) white female, aged 22, endo-extrabronchial, 5.0 cm., right stem bronchus, carcinoid pattern. Supposed complete bronchoscopic removal 22 years ago, followed by remission clinically and radiologically. Recurrence after 10 years with complete obstruction, conversion of right lung to cystic bronchiectasis. Radiation therapy. Present status, histology unchanged, living but disabled with hemorrhages and pneumonitis (Fig. 11).

Case 3: F.M., (U.C.H.) white male, aged 50, carcinoid pattern, extrabronchial, peripheral, 4 cm. Asymptomatic, observed 4 years. Died of ruptured aneurysm. Postmortem: Well encapsulated, no metastases.

Case 4: H.L., (U.C.H.) white female, aged 48, mixed tumor pattern, endo-extrabronchial, 5.0 cm., left stem and left upper lobe. Duration 25 years; left pneumonectomy $10\frac{1}{2}$ years ago. Present status, living and well, no metastases.

Case 5: I.W., (U.C.H.) and (S.F.H.) white male, aged 46, mixed tumor pattern, endobronchial, multiple polypoid tumors (2), long pedicles, 1 to 3 cm. and the other 2 cm., pedicles 2 mm. in diameter. Duration 6 years; complications empyema, pulmonary abscess, brain abscess, 74 bronchoscopic treatments, radon implantations. Death from brain abscess and pulmonary suppuration. Postmortem: no metastases.

Case 6: H.G., (U.C.H.) white female, aged 32, carcinoid pattern, endo-extrabronchial, 6.5 cm. intermediate and right lower lobe bronchi. Complications; empyema, abscess treated by surgical drainage. Radiation therapy. Duration 26 years, continued serious pulmonary hemorrhages and pneumonitis. Pneumonectomy attempted 1949 with resultant death. Postmortem showed no metastases.

Case 7: J.S., (U.C.H.) white male, aged 27, carcinoid pattern, intramural and endobronchial, 2 cm., right stem bronchus. Duration 6 years. Attempted bronchoscopic diathermy. Death 1 week after treatment. Postmortem: terminal pulmonary hemorrhage, septic cerebral emboli, no residual tumor or metastases.

Case 8: E.D., (U.C.H. and S.F.H.) white male, aged 13, carcinoid pattern, endobronchial, 2 cm., left stem. Duration 16 years. Bronchoscopic removal piecemeal, 6 years after no clinical recurrence, endomural lesion suspected.

Case 9: J.G., (U.C.H.) white male, aged 23, mixed tumor pattern, endobronchial with intramural extension, 2.5 cm., left stem bronchus, left pneumonectomy. Duration 13 months; died 1 month postoperative; no metastases.

Case 10: F.J., (U.C.H.) white female, aged 20, carcinoid pattern, endo-extrobronchial, 2.5 cm., left lower lobe. Duration 18 years. Left lower lobectomy. Ten and one-half years postoperative, patient living and well (Figs. 13 and 14).

Case 11: C.R., (U.C.H.) white male, aged 46, glandular pattern, endo-extrabronchial, 2.5 cm., left stem bronchus. Duration 13 years. Left pneumonectomy, complicated by empyema. Alive and well $10\frac{1}{2}$ years, since pneumonectomy.

Case 12: G.D., (U.C.H.) white female, aged 33, mixed tumor pattern, endo-extrabronchial, peripheral, 7.0 cm., left lower lobe. Duration 20 years. Left lower lobectomy. Alive and well $9\frac{1}{2}$ years after lobectomy (Figs. 4, 7 and 15).

Case 13: J.G., (S.L.H. and U.C.H.) white female, aged 21, carcinoid pattern, endo-extrabronchial, 5.0 cm., right stem and right upper lobe. Duration $10\frac{1}{2}$ years. Right upper lobectomy. Alive and well $9\frac{1}{2}$ years after lobectomy.

Case 14: S.J., (U.C.H.) white male, aged 49, probably mixed tumor, characteristic patterns not obtained; endo-extrabronchial, 7.5 cm., right stem and right upper lobe. X-ray therapy. One year later developed positive sputum. Duration 3½ years; followed 2½ years after treatment, alive and well then; no late followup.

Case 15: A.B., (U.C.H.) white female, aged 10, carcinoid pattern, endo-extrabronchial, 2.5 cm., left stem bronchus. Duration 37 years. First bronchoscopic removal with recurrence 5 years later, then bronchotomy with left lower lobectomy. Alive and well 4 years after bronchotomy and lobectomy; no metastases.

Case 16: W.C., (U.C.H.) white female, aged 46, no characteristic patterns obtained, probably carcinoid; endo-extrabronchial (peripheral), 4 cm., right lower lobe. Duration 20 years. X-ray therapy. Followup 10 years after x-ray therapy, condition good, occasional hemoptysis.

Case 17: C.B., (U.C.H.) white female, aged 34, probably carcinoid characteristic patterns not obtained; endo-intramural, undetermined size, right upper lobe and right stem bronchus. Duration 17 years. Radiation therapy. Followup 10 years after radiation therapy, condition good.

Case 18: D.W., (U.C.H.) white female, aged 41, no characteristic patterns obtained, probably carcinoid; endo-extra bronchial, 5 cm., left upper lobe and left stem. Duration 7 years. Radiation therapy. No followup after 1 year following radiation; good condition at that time.

Case 19: E.A., (U.C.H.) white female, aged 25, mixed tumor pattern, endo-extrabronchial, 7 cm., right middle lobe. Duration 18½ years. Right middle lobectomy. Nine years after lobectomy, alive and well.

Case 20: D.C.H., (S.F.H.) white male, aged 30, carcinoid pattern, endo-intramural, 3 cm., right upper lobe. Duration 10 years. Piecemeal bronchoscopic removal. Nine years later apparently well, endomural tumor suspected.

Case 21: D.M., (U.C.H.) white female, aged 40, carcinoid pattern, endo-extrabronchial, 3 cm., intermediate bronchus. Duration 8½ years. Right lower and middle lobectomy. Alive and well 8½ years after multiple lobectomy, no metastases.

Case 22: I.S., (U.C.H.) white female, aged 28, carcinoid pattern, endo-extrabronchial, 3 cm. Duration 8 years. Left pneumonectomy. Alive and well 7 years after left pneumonectomy; no metastases.

Case 23: K.F., (C.L.H.) white female, aged 30, mixed tumor pattern, 7 cm., endo-extramural, intermediate bronchus, right lower lobe. Duration 3 years. Multiple lobectomy, right middle and lower lobes. Alive and well 3 years; metastases to regional mediastinal lymph nodes (2), invasion inferior pulmonary vein.

Case 24: L.B., (B.V.H.) white male, aged 60, carcinoid pattern, endo-extrabronchial, 5 cm., right stem bronchus and right lower lobe. Duration 30 years. Complications, draining sinus 20 years with empyema and abscess, carcinoma of bladder, chronic lymphatic leukemia, pulmonary tuberculosis. Right pneumonectomy. Alive but had a recent re-entry because of tuberculous empyema with a spread into the remaining left lung. Prognosis, bad, because of pulmonary tuberculosis, 1 regional mediastinal node involved.

Case 25: A.K., (B.V.H.) white male, aged 25, mixed tumor pattern, endo-extrabronchial, peripheral, 7 cm., left lower lobe. Duration 4 years. Left lower lobectomy. Alive and well 3½ years after left lower lobectomy. Metastases to 1 regional lymph node.

Case 26: F.H., (B.V.H.) white male, aged 30, carcinoid pattern, endo-extrabronchial, 5 cm., left stem and left lower lobe. Duration 7 years. Alive and well 3 years after left pneumonectomy.

Case 27: P.O.P., (B.V.H.) white male, aged 50, carcinoid pattern, extrabronchial (peripheral), 5 cm., right upper lobe. Duration 4½ years. Alive and well 3½ years after right pneumonectomy.

Case 28: R.B., (C.L.H.) white female, aged 32, carcinoid pattern, endo-intramural, 2 cm., right middle lobe. Duration 6 years. Right middle lobectomy. Alive and well 3½ years after lobectomy.

Case 29: S.B., (C.L.H.) white female, aged 60, carcinoid pattern, endobronchial, large extrabronchial mass, with destroyed left lung suspected. Duration uncertain. Treatment, none. Metastases in the liver, probable, not yet proven.

Case 30: M.B., (C.L.H.) white female, aged 40, carcinoid pattern, endo-extrabronchial, right lower lobe, 4 cm. Duration uncertain, probably more than 1 year. Right lower lobectomy. Alive and well 3 months; metastases to 1 regional lymph node.

Case 31: S.N.M., (C.L.H.) white female, aged 65, carcinoid pattern, endo-extrabronchial, undetermined (probably about 5 cm.), left stem bronchus. Duration 30 years. Bronchoscopic removal 15 years ago followed by radiation therapy; now has destroyed left lung and 2 nodules in the right lung, probably metastatic, not yet proven. Present status, tumor histology unchanged by bronchoscopic biopsy, debilitated and weak. Prognosis, poor.

Case 32: A.H., (U.C.H.) white male, aged 40, mixed tumor pattern, endo-extrabronchial, with marked infiltration several cm. intramurally along the bronchial wall, located bilaterally at the carinal area. Duration 5½ years. Bronchoscopic removal begun 5 years before death, radiation therapy. Death from asphyxia. Postmortem: recurrence of metastases in the pleura, lung and liver (Fig. 5).

Case 33: E.S., (C.L.H.) white male, aged 52, mixed tumor pattern, endo-extrabronchial with extensive infiltration intramurally, bilaterally at the carina. Duration 6 years. Bronchoscopic removal 6 years before death. Death from asphyxia, 3 months after bronchotomy to improve the airway. Postmortem: recurrence with definite malignancy; metastatic implants on the pleura; invasion of the esophagus.

Case 34: S.S., (C.L.H.) white female, aged 37, carcinoid pattern, original tumor unknown size, located in bronchus. Bronchoscopic removal elsewhere 7 years before. Duration 8 years. Recurrence with tension emphysema of the right lung, tumor 2 cm. in diameter, 1.0 cm. sessile attachment to mesial wall of carina. Right transpleural bronchotomy. Alive and well 4 months, atelectasis of right lung completely cleared, aeration good (Figs. 8, 20, 21).

Case 35: A.P., (H.G.H.) white female, aged 14, glandular pattern, 4 cm., pedicle 4 mm. endobronchial, left stem bronchus. Duration 2 years. Transpleural bronchotomy 1 year ago; left lung now clear, well aerated. Recent bronchoscopy, no sign of recurrence (Figs. 6, 18, 19).

Case 36: B.P., (C.L.H.) white male, aged 26, carcinoid pattern, endo-extrabronchial, 5 cm., bifurcation of left stem bronchus. Left pneumonectomy 1 year ago. Duration 6 years. Since pneumonectomy, patient well and working.

Case 37: J.R., (C.L.H.) white female, aged 40, carcinoid pattern, endo-extrabronchial, 4 cm., intermediate bronchus and right lower lobe. Duration 6 years. Complications empyema and lung abscess requiring surgical drainage 6 months before multiple right lower and right middle lobectomy one year ago. Living and well, working, no metastases (Figs. 10, 16, 17).

Case 38: L.S., (C.L.H.) white female, aged 16, carcinoid pattern, 8 cm., right lower lobe and intermediate bronchus. Duration 30 years, empyema drained at onset, followed by thoracoplasty. Attempted bronchoscopic removal, followed by radiation therapy, ten years before death. Death was associated with pituitary dysfunction and serious diabetes mellitus. Post-mortem examination showed persistent pulmonary suppuration with bronchocutaneous fistula, recurrent tumor, pituitary adenoma, pinealoma, thyroid adenomata, bilateral adrenal adenomata, cor pulmonale, metastases to regional mediastinal lymph nodes, invasion of pulmonary vessels, suppuration and destruction of right lung.

C.L.H.—Cedars of Lebanon Hospital, Los Angeles, California.
U.C.H.—University of California Hospital, San Francisco, California.
H.G.H.—Harbor General Hospital, Branch of Los Angeles County General Hospital, Torrance, California.
S.F.H.—San Francisco City and County Hospital, San Francisco, Calif.
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Metastatic Tumors of the Lung

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Some years ago when the author first called attention to the promising potentialities of mass x-ray surveys for the early discovery of carcinoma of the lung, vociferous criticism coming from conservatively conditioned medical quarters greeted his idea. In contrast, today, experience gained from millions and millions of survey films of the chest has vindicated this proposition beyond the shadow of a doubt. Needless to say that the same principle applies to the early detection of metastatic tumors of the lung. Small or moderate-sized metastatic neoplasms may exist without symptoms. The same holds true, to a certain extent, of small nodular forms widely scattered in the lung and, in some cases, of large metastatic newgrowth.

Of course, in a great many instances, disturbing symptoms prompt the patient to seek medical attention. The symptoms are the usual ones encountered in a number of infections, allergic, circulatory and primary neoplastic diseases of the respiratory tract. There may be a persistent, unproductive, hacking cough when pulmonary metastasis first develops. When bronchopneumonia, lung abscess or bronchiectasis complicates the picture, there is ample mucopurulent, purulent or foul sputum. It is well carefully to examine the expectorated material. It may contain food particles when communication is established between a carcinomatous esophagus and a bronchus. Wheezing may result from intense edema of the bronchial mucosa; also, it may be brought about by intrabronchial growth or by compression of the bronchus by tumor masses or by enlarged lymph nodes. Metastatic chorionepithelioma and hemangioma are associated with frequent and, often, large pulmonary hemorrhages. In other metastatic tumors, hemorrhage is less common. It varies from blood-streaked sputum to large quantities of blood.

Pain may be an early symptom. On the other hand, it may be entirely absent during the entire course of the disease. Some patients complain of pain in the substernal or axillary region. It may be dull, aching or lancinating. It may radiate to the shoulder or to the back. It is exaggerated by deep breathing and by coughing. Not infrequently, it is more pronounced at night.

Dyspnea may result from pleuropulmonary changes or from pathologic involvement of the surrounding structures. In this

regard, reference should be made to extensive loss of lung parenchyma due to the presence of tumor masses; compression of the trachea or major bronchi; secondary infection; plastic pleurisy associated with chest pain; large pleural effusion; spontaneous pneumothorax; paralysis of the phrenic nerve; neoplastic infiltration of the heart and the pericardium; obstruction of the large thoracic veins; severe anemia attributable to the toxic effect of the newgrowth. Simultaneously, various degrees of cyanosis are noted, with possible swelling of the neck.

General toxic effect of the tumor may induce malaise, anorexia and loss of weight. Also, pallor, moderate or high fever may be noted, particularly in the presence of secondary pulmonary infection.

Of all metastatic tumors of the lung, *carcinoma* is the most frequent. It may originate from practically any part of the body. The route of its spread is either direct hematogenous, indirect hematogenous via the thoracic duct, per contiguity or through the hilar lymph nodes. In the latter instance, the neoplasm spreads through retrograde extension. Pathologically, the following forms are distinguished: (1) Large, spheroid, multiple, more or less symmetrical, bilateral, sharply delimited masses, with or without associated enlargement of the hilar and mediastinal lymph nodes. (2) Miliary nodules in both lungs, with lymphangitis carcinomatosa. (3) Solitary tumor masses in one or both lungs. (4) Enlarged hilar and mediastinal lymph nodes, with carcinomatous infiltrative extension into the lung ("rising sun" appearance). (5) Pleural involvement.

On postmortem examination, lymphangitis carcinomatosa is characterized by a relief-like, grayish appearance the anatomic location and arrangement of which corresponds to the pattern of the pulmonary lymphatics. Alongside these elevated structures there are gray nodules which measure from 3 to 30 mm. in diameter. Microscopic inspection reveals carcinoma cells in the lymph vessels, along the bronchi and in some of the blood vessels. The latter may be completely obliterated by thrombi which contain tumor cells.

Recent studies have offered convincing proof that the so-called hypernephroma is not a special clinical or pathologic entity but only a variety of carcinoma of the kidney.

Sarcoma, regardless of its location, has a pronounced tendency to pulmonary metastasis. Histologically, it consists of connective tissue cells which may be encountered in three forms: (1) small or large spindle cells; (2) giant cells; (3) round cells. This neoplasm has a rich blood supply. Metastasis take place through the blood stream.

Another tumor which shows a high tendency to metastasize to the lung is *osteogenic (osteoblastic) sarcoma*, also known as osteosarcoma. The most frequent location of the primary tumor is in the long bones of the lower extremities.

Also, metastasis to the lung is common in *Ewing's tumor* (solitary diffuse endothelioma), (endothelial myeloma), (nonosteogenic embryonal osteoblastoma, Heublein). The long bones, particularly the tibia and fibula, are the most frequent sites of the primary growth. In some instances, metastasis in the lung was found several months after the amputation of the diseased extremity.

The lung is a favorite site of metastasis for *Wilms' tumor*, which is also known as embryoma of the kidney, embryonic nephroma and nephroblastoma. It consists of undifferentiated or incompletely differentiated embryonic renal tissue. Usually, the tumor is found in infants and children.

Liposarcoma may originate from normal fat tissue or from a lipoma. The primary tumor is found in the lower extremities, abdomen, face, neck, arms or elsewhere. It is seen mostly in persons of middle or advanced age. Pulmonary metastasis may be observed several years after the identification of the primary neoplasm.

Pulmonary manifestations of *Hodgkin's disease* result from metastasis in 90 per cent of the cases. Most frequently seen forms of this condition are: (1) Extension of Hodgkin's disease from hilar lymph nodes after rupture of their capsule, with consequent direct infiltration of adjacent alveoli. (2) Spread of the disease along the interlobular, peribronchial and perivascular lymphatics in fan-like fashion. (3) Miliary nodules evenly distributed throughout both lungs. The components of the infiltration encountered in Hodgkin's disease show a pleomorphic appearance on histologic examination. The alveoli as well as the supportive tissues of the lung may be filled with lymphocytes, plasma cells and characteristic mononuclear or multinuclear giant cells. The latter should be properly designated as Greenfield cells but they are habitually, though erroneously, called Sternberg or Dorothy Reed cells by virtually all high priests of Pathology. This is done in face of the chronicles of medical history which tell us that the first description of these cells by Greenfield of Great Britain was recorded twenty years before the report of the Austrian Sternberg and nearly a quarter of a century prior to the communication of Reed of Baltimore.

Chorionepithelioma arises from the covering of chorionic villi, usually from the fundus of the uterus, although cases with primary sites unrelated to the genital organs have also been reported. Highest percentage of these tumors is found in hydatidiform

moles but in a substantial number of instances, it is encountered in connection with normal or ectopic pregnancy or its development may follow abortion. Abnormal proliferation of the syncytial cells leads to the formation of neoplasm. In view of the abundant blood supply which surrounds the chorionic villi, there is ample opportunity for the tumor cells to pass through the uterine veins and thus be transported to the lung.

Mixed tumors of the uterus may develop from malignant transformation of a uterine adenomyoma. The metastatic foci in the lung show all the characteristic earmarks of uterine structures.

Dysgerminoma of the ovary is another tumor which may cause metastasis in the lung. The ovarian newgrowth develops from undifferentiated germinal cells. The primary lesion is bilateral in nearly one-third of the cases. Clinically, it is seen in young adults but it may occur in the adolescent and in the aged. Dysgerminomas usually attain large size before they metastasize. Histologically, the tumor is composed of strands of large, uniform epithelial cells surrounded by narrow or wide channels of fibrous tissue which contains lymphocytes.

Granulosa Cell Tumors arise from normal follicular tissue or from the undifferentiated stroma of the ovaries. They are found as white or yellowish, solid neoplasms which may be discovered clinically while their size is still small or when they attain excessive growth.

Arrhenoblastoma is an ovarian tumor associated with masculinization. It occurs in women between the ages of 20 and 40 years; very rarely in adolescents and in the aged. The tumor is of solid consistency or cystic. Histologically, it is characterized by tubular glandular structure.

Localization of metastasis of *malignant tumors of the testicle* is common in the lung. These include embryonal carcinoma, seminoma and teratoma. Their highest incidence is observed between 20 and 40 years of age. Metastasis may be discovered before or after apparently adequate treatment of the primary neoplasm.

It is beyond the purpose of this presentation to assay in details all of the pertinent characteristics of tumors which may form pulmonary metastasis. But it is well to enumerate them. The list includes the following:

Adamantinoma,
Adenoacanthoma of the uterus,
Chloroma,
Chondrosarcoma,
Grape-like sarcoma of the vagina,
Nonmalignant metastasizing hemangioma,
Hemangioendothelioma,
Leiomyosarcoma of the uterus,

Malignant hepatoma (carcinoma of the liver),
Melanoma,
Meningioma of Cushing (arachnoid fibroblastoma of Mallory),
Myeloma,
Myeloblastoma,
Neuroblastoma,
Papilloma of the larynx,
Synovioma.

Diagnosis

Success in accurate diagnosis is predicated upon the resourcefulness and acumen with which all possible sources of information are explored. One should investigate the incidence of malignant tumors in the patient's family. Occupational hazards which are capable of provoking tumor formation should be ascertained. In women, history of abnormal gestation or irregular vaginal bleeding may point toward the origin of pulmonary metastasis. Chorionepithelioma should be thought of when there is vaginal discharge of grape-like, transparent vesicular structures. Also, subjective and objective symptoms and signs of endocrine imbalance may guide one toward finding the site of the primary tumor.

On physical examination, the Hare-Horner-Claude Bernard syndrome may be noted when the metastatic lesion is localized in the apical region. One should look for the sentinel nodes of Troisier and Virchow in the supraclavicular fossae. Signs of obstruction of the superior vena cava may be encountered in massive neoplastic changes of the upper mediastinum. Limitation in the respiratory excursions of a hemithorax should call one's attention to a unilateral lung lesion and its possible sequels, such as massive atelectasis, large hydrothorax or localized emphysema. In some cases, the Oliver-Cardarelli sign is easily detectable. Clubbing of the fingers may be present. These changes in the digits are far from being characteristic of metastatic lung tumors. They may be seen in connection with any of the primary neoplasms of the lung (benign or malignant); also, in lung abscess, tuberculosis, nontuberculous pulmonary fibrosis, chronic bronchitis, bronchial asthma, arteriovenous fistula of the lung, emphysema, congenital cystic disease of the lung, empyema, malignant tumors of the pleura, mediastinal neoplasms, congenital heart disease, subacute bacterial endocarditis, chronic valvular lesions of the heart with decompensation, cachexia stumipriva, amyloidosis, syphilis, chronic liver disease, chronic kidney disease, ulcerative colitis, amebic dysentery and intestinal polyposis. Moreover, clubbing of the fingers may be familial.

Large tumors are easily detectable by dull percussion note, decreased pectoral fremitus and absent breath sounds over the

corresponding area. Small neoplasms are likely to be missed on physical examination unless they cause massive atelectasis or obstructive emphysema of one lung. These conditions, if otherwise unexplained, should focus one's attention on possible neoplastic growth. Inasmuch as areas of atelectasis are predilectional sites for pathogenic micro-organisms, bronchopneumonia, infected bronchiectasis or lung abscess may develop as a complication of a small newgrowth. It is a good axiom never to be satisfied with the diagnosis of bronchiectasis or lung abscess until their origin has been ascertained with reasonable certainty. Also, it is well to keep in mind that unilateral bronchitis is always highly suspicious of bronchial obstruction. When metastatic lung tumors appear in the form of widespread, bilateral miliary nodules, the percussion note over the chest is likely to be hyperresonant on account of the ensuing compensatory emphysema.

General physical examination may reveal the presence of tumor mass in the scrotum, enlarged inguinal lymph nodes, pelvic or abdominal masses, enlargement of the uterus, stone-like induration of the prostate, ascites or swelling along the shaft of long bones. Gastro-intestinal x-ray studies with barium or double contrast medium may show the primary site of the neoplasm. Special attention should be paid to the passage of the barium through the esophagus so as to detect stenosis due to carcinoma of this structure or to extrinsic pressure by a mediastinal mass. Swallowing small capsules filled with carmin may be followed by expectoration of red-stained sputum indicating communication between the carcinomatous esophagus and the respiratory tract. Urograms are of value in locating neoplastic growth in the kidneys and bladder.

Fluoroscopic examination and roentgenograms of the chest taken in various projections reveal the metastatic tumor either as a single opacity or as multiple shadows. Multiple shadows are five kinds: (1) Miliary nodules widely distributed throughout both lungs. (2) Snow flake-like, small opacities of the same distribution. (3) Ill-defined shadows up to 3 cm. in diameter scattered in both lung fields. (4) Sharply demarcated, dense, round shadows, varying in size from that of a quarter to a 50 cent piece (from 23 to 30 mm.). (5) Massive, well-defined, somewhat oval shadows which are much larger than the ones just mentioned. Miliary nodulations in the roentgenogram of the chest may be encountered in a number of other conditions. The enumeration of the latter may be helpful in the differential diagnosis of this type of metastatic tumors.

Miliary abscesses,
Pulmonary acariasis,

Pulmonary adenomatosis,
Miliary amyloidosis,
Bagasse disease,
Berylliosis,
Bronchiolitis,
Miliary bronchopneumonias, including certain forms of virus infection,
Bouillaud's disease,
Cave sickness,
Lymphatic leukemia,
Melioidosis,
Periarteritis nodosa,
Purpura hemorrhagica,
Schistosomiasis,
Syphilis with miliary gummas,
Miliary tuberculosis,
Collagen diseases,
Congenital miliary cysts,
Pulmonary edema,
Fungus infection,
Residuals following pulmonary hemorrhage,
Pulmonary hemosiderosis,
Eosinophilic leucocytosis,
Residuals of multiple small pulmonary infarctions,
Iodized oil retained following bronchogram,
Lipoid pneumonia,
Paragonimiasis,
Polycythemia vera,
Sarcoidosis,
Silicosis and other pneumoconioses,
Tropical eosinophilia,
Essential xanthomatosis.

A shadow cast by a solitary tumor may be localized in any part of the lung. It may be peripheral or central. Neoplasms centrally located present an opacity which is fused with that of the hilar structures, particularly, when there is secondary involvement of the lymph nodes in this region. Solitary tumors lying in the lung field are usually well delineated. In some instances their border is hazy on account of perifocal hemorrhage. Perihilar neoplasms cast a shadow or irregular, infiltrative outline. To determine the exact location of some of the larger basal tumors and also, to differentiate them from eventration of the diaphragm, diaphragmatic hernia and subdiaphragmatic disease, it may be necessary to give the patient barium for the visualization of the gastrointestinal tract. Diagnostic pneumoperitoneum may be called for.

Large tumor masses occasionally show rarefection in their center, which is indicative of cavity formation. This possibility requires its differentiation from cavities seen in various lung infections, particularly in lung abscess, tuberculosis and fungus infection and

possibly in syphilis and silicosis. Other conditions to be kept in mind in this connection are: congenital cystic disease of the lung, cystic emphysema in pneumonia, echinococcus cyst, simple mediastinal cyst and mediastinal gastric cyst.

Standard roentgenograms of the chest should be studied for the presence of erosion of the bony structures. An associated large pleural effusion may entirely obscure the underlying neoplasm. It is mandatory to remove the effusion by aspiration for the purpose of determining its specific gravity, cell content, with special emphasis on search for malignant cells, and other properties which are of diagnostic interest. Also, removal of the fluid permits better visualization of the lung fields. In some instances, valuable information can be gained by replacing some of the aspirated fluid with air and then do a thoracoscopic examination. Bronchography may give not only good topographic orientation but also it demonstrates coexistent bronchial stricture, occlusion or bronchiectasis.

Examination of biopsy specimens is of cardinal importance in the diagnosis of metastatic tumors of the lung. These can be secured by bronchoscopic approach or by obtaining sections from involved lymph nodes in the neck or axilla. Cytologic examination of the sputum or material obtained by bronchoscopic aspiration is applicable in the diagnosis of metastatic carcinoma of the lung as it is being used in primary bronchogenic cancer. When other procedures fail to solve the diagnostic problem, exploratory thoracotomy is the best way to clarify the situation. With modern surgical technique, exploratory thoracotomy entails less risk than exploratory laparotomy.

Metastatic malignant tumors of the testicle and chorionepitheliomas are accompanied by an increase in gonadotropic hormones. Repeated assaying of these hormones is a useful adjunct in following the course of the disease after surgical removal of the tumor. In chorionepithelioma of the male, both breasts are enlarged and contain freely moveable, nontender masses. The pectoral swelling can be easily mistaken for bilateral mastitis. On closer examination, however, one finds that colostrum can be expressed from the nipples. In some of these cases, colostrum formation may be slight or entirely absent, because considerable time is necessary for the functional hypertrophy of the male breast under the influence of hormones liberated from the tumor.

Some clinicians recommend a therapeutic test with x-ray irradiation. Chorionepithelioma, Ewing's tumor, malignant tumors of the testicle and other metastatic neoplasms are highly radiosensitive.

Prognosis

There are great variations in the behavior of metastatic newgrowth of the lung. Even so ,malignant tumors of this organ should be looked upon with grave anticipations. Such attitude is particularly justifiable when there are multiple foci of metastasis. The prospects are more favorable in women with chorionepithelioma. In such instances, even extensive metastatic lung involvement may completely clear after hysterectomy for the primary neoplasm.

Treatment

Evidence is accumulating in support of surgical removal of solitary metastatic lung tumors. Depending upon given circumstances, lobectomy or pneumonectomy are the types of intervention advised. Old age in itself is no contraindication to thoracic surgery, provided cardio-respiratory incompetence, renal failure, metastasis to other organs and inoperability of the primary tumor do not interdict it. Surgical intervention may be required from a few months to over ten years after the removal of the primary neoplasm. Observations on the length of survival following these operations are favorable and justify wider application of this method of treatment. Pronounced regression may be attained by x-ray irradiation of metastatic pulmonary foci in the aforementioned radiosensitive tumors. X-ray irradiation is permissible as a palliative measure when the primary tumor is inoperable or the patient declines surgical intervention. Of course, the prerequisite of such treatment is the radiosensitiveness of the newgrowth.

In view of the observation that in some instances, carcinoma of the breast has more malignant tendencies during pregnancy, it was advocated that oophorectomy should be performed to exert a suppressive influence upon breast cancer and its metastatic foci. Also, the administration of testosterone propionate and x-ray irradiation of the ovaries has been practiced for the same purpose.

SUMMARY

Experience shows that metastatic tumors of the chest occur with greater frequency than generally realized. For this reason, it is mandatory to consider them as a diagnostic possibility when one is dealing with an apparently obscure diagnostic chest problem. In connection with the discussion of various neoplasms which may form pulmonary metastasis, the following items deserve particular attention.

1) The symptomatic manifestations of metastatic tumors of the chest are, in general, the same as those of primary malignant newgrowths.

2) In the diagnostic assaying of the patient due attention should be given to the past medical history, physical and x-ray findings, with special reference to a thorough search for coexistent primary tumor and enlarged superficial, peripheral lymph nodes.

3) Examination of biopsy specimens secured bronchoscopically or otherwise is of cardinal importance.

4) Exploratory thoracotomy should be resorted to when other diagnostic methods fail.

5) Surgical removal of solitary metastatic chest tumors is a feasible procedure, provided the patient's general condition is satisfactory and there is no contraindication to major chest surgery because of the inoperability of the primary tumor or the presence of metastasis in other organs.

RESUMEN

La experiencia demuestra que los tumores metastáticos en el tórax, ocurren más a menudo de lo que generalmente se creía. Por esta razón es imperativo considerarlos como una posibilidad diagnóstica cuando se trate de un problema de obscuro en el tórax.

Respecto de los varios neoplasmas que pueden tener metástasis pulmonares, los siguientes merecen especial atención.

1) Las manifestaciones sintomáticas de las metástasis en el tórax son en general las mismas de los tumores malignos primitivos.

2) En el balance diagnóstico de los enfermos debe ponerse la debida atención a la historia clínica, hallazgos clínicos y radiológicos con especial cuidado en lo referente a la investigación completa de un tumor primario coexistente y ganglios crecidos superficiales.

3) El examen de especímenes de biopsia obtenidos por broncoscopia o de otra manera, es de importancia cardinal.

4) Cuando todos los demás métodos fallan hay que recurrir a la toracotomía exploradora.

5) La extirpación de los tumores metastáticos del tórax es practicable siempre que el estado general sea satisfactorio y no haya contraindicaciones de operabilidad del tumor primario o metástasis en otros órganos.

The Surgical Treatment of Carcinoma of the Esophagus

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Thirty-seven years ago Torek[1] reported the first successful transthoracic resection of the esophagus for carcinoma. As a result, clinical interest in the possibilities of successful surgical treatment of this disease was awakened, only to languish and almost disappear in the following twenty-five years. During this period of one quarter of a century, many modifications of the technique of Torek were devised, in some instances with considerable success. Nevertheless, surgical interest waned markedly as a result of experiences with high operative mortality, forbidding morbidity, unsatisfactory functional results, and low five-year survival results. Consequently, there was once more little surgical activity directed toward a definite effort to cure esophageal cancer when, in 1938, Adams and Phemister[2] reported a new technique for transthoracic resection of carcinoma of the lower esophagus. This method consisted of removal of the lower esophagus with an anastamosis of the upper esophagus to the stomach, a feat made possible by the interruption of the left gastric artery, the left gastro-epiploic artery, the vasa brevia, and the mobilization of the stomach along the lesser and greater curvatures so that it might be delivered into the thorax in order that continuity could be restored by a union of this organ to the esophagus at the level of division well above the neoplasm. This was accomplished by means of a thoracic approach coupled with laparotomy through the diaphragm.

The contribution of Adams and Phemister has already proven to have been monumental. An immediate re-awakening of interest and effort in the surgical treatment of this disorder was the primary result, and at the same time, a new approach was provided for the surgical correction of carcinoma of the gastric cardia. Tremendous credit for essential, priceless pioneering in this work must also be accorded Sweet[3-5] and Garlock[6-9] for their invaluable contributions to the evolution and advancement of surgical measures to be employed in the surgical attack upon esophageal malignancy, one of the most distressing and harrowing cancers to which

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man is vulnerable. One might say that progress was made in retrograde direction in this matter since, in a short period of years, the principles of Adams and Phemister have successively been applied to lesions occurring at higher and higher levels of the esophagus so that by now, carcinoma at any level has been mastered from a surgical standpoint. These triumphs have been made possible by resection of the esophagus from a point well above the neoplasm, down to the stomach, and by immediate restoration of alimentary tract continuity through the device of esophagogastrostomy or even pharyngo-gastrostomy.

These techniques constitute a direct attack upon the neoplasm with immediate restoration of continuity. The functional results are very favorable. Operative mortality in competent hands has been steadily reduced so that surgical deaths can be expected to occur in about fifteen per cent of the patients, the figures breaking down into a result somewhat lower than this for lesions of the lower third of the organ, and slightly higher for cancer of the upper esophagus. These achievements have not been in widespread use long enough to permit a reliable statistical analysis which would provide a representatve experience in five-year survival rates. Nevertheless, Sweet[5] has stated that his own series of patients with this disease provide sufficient indication in this respect for a safe prediction on his part that the five-year survival rate will compare favorably for carcinoma in other internal viscera. Most deaths which result from progression of cancer occur within two years after operation and experience has demonstrated that recurrence at the site of the anastamosis of the stomach to the esophagus is extremely rare.

The most imposing hurdle to more rapid progress in the successful management of patients having esophageal cancer or gastric carcinoma at the cardia is delay in diagnosis. Most of these victims still fail to seek medical attention until complete obstruction of the esophagus has occurred or is imminent. The surgical principles of radical "en bloc" resection cannot be applied to the removal of the esophagus because of the intimate proximity of vital structures along its course. Earlier diagnosis is absolutely mandatory in order that definitive treatment may be administered at a time before local extension of the neoplasm has advanced beyond the confines of the esophagus.

The diagnosis is seldom difficult. The cardinal symptom of dysphagia merits immediate investigation in any patient presenting the complaint. If due to esophageal malignancy, a deformity in the lumen of the organ can be demonstrated in an esophagram in almost every instance. Experience has shown that it is a valuable expedient to advise the examining roentgenologist that a

lesion of the esophagus is suspected. Endoscopic examination with the esophagoscope then will make it possible to confirm the diagnosis by means of a biopsy. Lesions which obstruct the lower end of the organ are sometimes due to extension of cancer of the gastric cardia and in such instances the biopsy will usually reveal adenocarcinoma while those neoplasms arising in the esophag s are of the epidermoid type. In our experience, an occasional such lesion of the gastric cardia causes esophageal obstruction by extension in the wall of the lower end of the esophagus but without involvement of the mucosa, thus defying attempts to secure a representative tissue biopsy. Under such circumstances, exploratory thoracotomy is required in order that the diagnosis may be sustained and appropriate treatment rendered. It is to be emphasized that instances of the latter type must not be dismissed from consideration without exploratory operation because of a negative biopsy obtained at esophagoscopy.

The diagnosis of cancer of the esophagus is the indication for

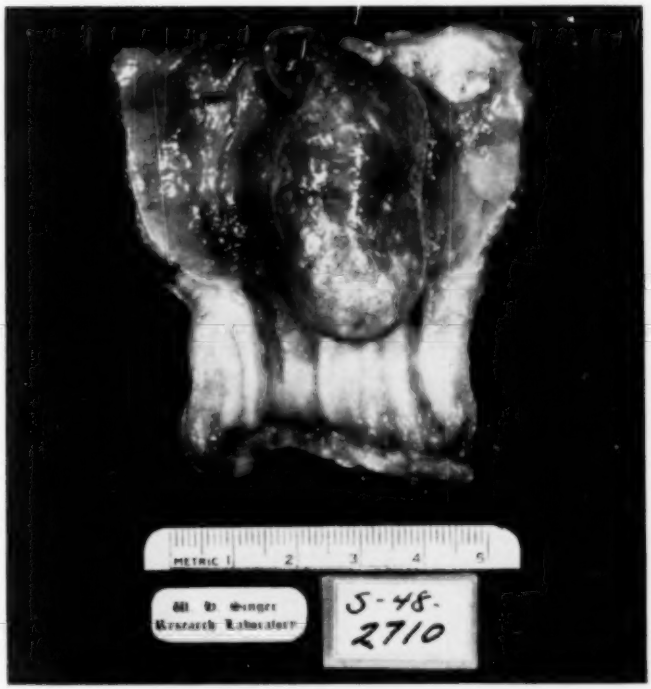


FIGURE 1: Epidermoid carcinoma (squamous cell type) of esophagus, papillary type (resected specimen).

operation. Contraindications to the adoption of a plan of resection surgery include proven metastases such as those to accessible regional lymph nodes or to the liver, the latter being established with some consistancy when suspected clinically by means of an aspiration biopsy of the liver. Persistent pain, usually in the back, indicates extension beyond the limits of the esophageal wall and often will contra-indicate an operation. Continuous fever is another finding which militates against an effort to perform resection, and is due to an extensive, infected, ulcerating cancer. Age alone is seldom a valid objection to surgery in these patients but the general state of the individual must be evaluated from the standpoint of surgical risk before the patient is accepted for an operation.

Most esophageal neoplasms are sessile or ulcerative in character, however, an occasional papillary epidermoid carcinoma is encountered (Figure 1). In this instance, the symptom of dysphagia had been present and slowly progressive over a period of three years.

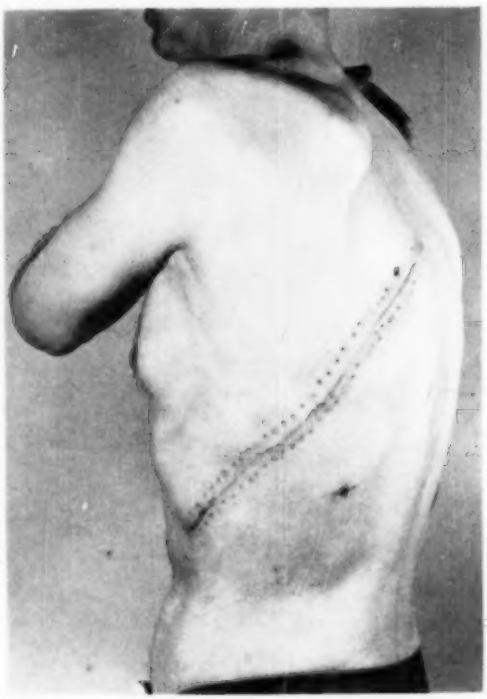


FIGURE 2: Photograph of patient showing scar of incision employed in resecting eighth left rib to gain entry into thorax.

A successful resection of the lower esophagus and esophagogastrostomy was followed by death fourteen months later due to extensive metastases to the liver without demonstrable evidence of local recurrence or other metastases.

The Surgical Management of Carcinoma of the Lower Esophagus and the Gastric Cardia

The left transthoracic approach coupled with opening the diaphragm provides easiest access to the esophagus and stomach for a resection of the lower esophagus (below the arch of the aorta) and carcinoma of the gastric cardia. A sub-periosteal resection of the entire eighth rib (Figure 2) permits ample exposure of the operative field for tumors at this level, the underlying pleura then being incised, and a rib spreader put in place. Exploration of the esophageal lesion to determine resectability can be performed before the diaphragm is opened. Having established the presence of favorable conditions in this respect, the left leaf of the diaphragm is incised from a point near the lateral margin to the hiatus (Figure 3). At this time, abdominal exploration can be done to determine the operability of a cancer at the cardiac end of the stomach and to establish the stage of the disease in such gastric lesions; the same is true in cancer of the esophagus. A search for metastases is made, special emphasis being placed upon pal-

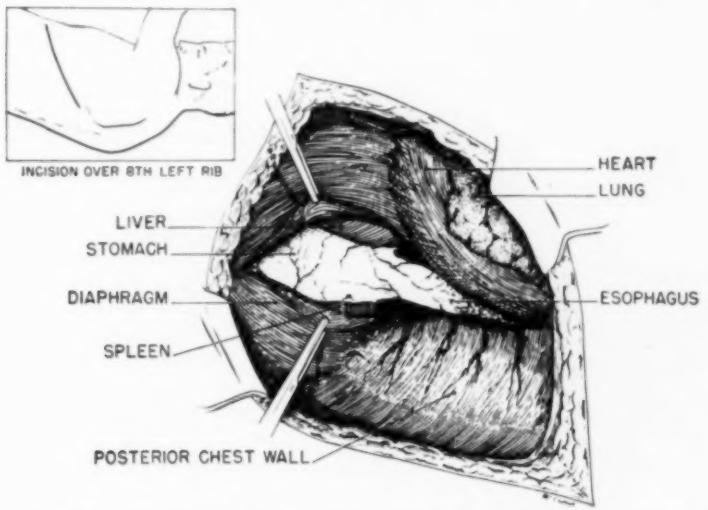


FIGURE 3: Transthoracic, transdiaphragmatic approach to lower esophagus and gastric cardia, mobilization of lower esophagus has been initiated and stomach, spleen and liver are visible through diaphragmatic laparotomy incision.

pation of the liver, and upon examination for evidence of lymph node metastases, notably to those about the left gastric artery and to nodes along the lesser curvature. Examination for evidence of extension producing a "rectal shelf" is likewise carried out. Advanced extension to regional nodes, evidence of liver metastases, and a "rectal shelf" are all considered contra-indications to resection. Figure 4 represents a diagrammatic illustration of the regional nodes which may be involved in esophageal cancer.

Once the decision has been made to proceed with resection, mobilization of the esophagus is completed to a point high enough to permit division and anastamosis at a point well above the growth, preferably two inches or more from the top level of the lesion as demonstrated by palpation and inspection. The arterial supply to the esophagus must be borne in mind during the mobilization of the organ (Figure 5).

Attention is then directed at mobilization of the stomach by

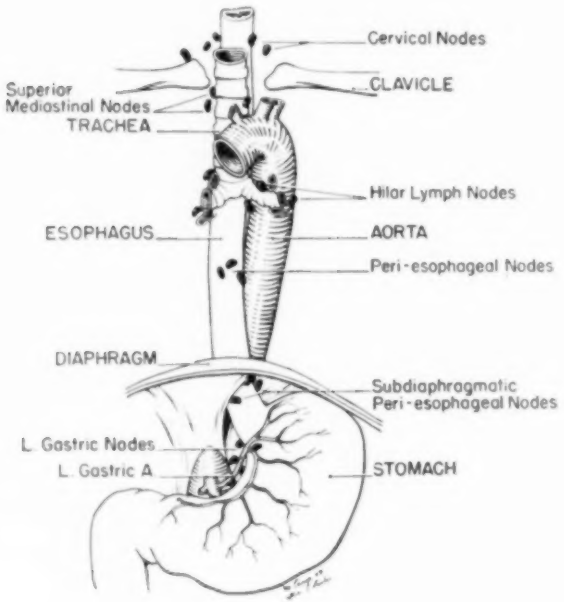


FIGURE 4: Diagrammatic illustration of cervical, mediastinal and abdominal lymph nodes intimately associated with lymph drainage of the esophagus. (Redrawn by M. Croup from M. McLatchie, Sweet, R., Surgery, 1948).

freeing the greater and lesser curvatures. The distance one must proceed along the greater curvature will vary with the level the stomach must reach in the thorax but complete division is usually necessary along the lesser curvature for satisfactory delivery of the stomach. The vessels along the margins of the curvatures must be maintained so that the blood supply may be preserved to the entire organ from the right gastric and right gastro-epiploic arteries (Figure 6). The vasa brevia must be divided and ligated on the greater curvature. The left gastric artery is ligated and divided at a point as far from the stomach as possible so that the bulk of the peri-arterial nodes will be left on the stomach, to be removed later either by dissection or by transection of the organ when the latter is required. The stomach is then delivered into the thorax (Figure 7) and divided from the esophagus at

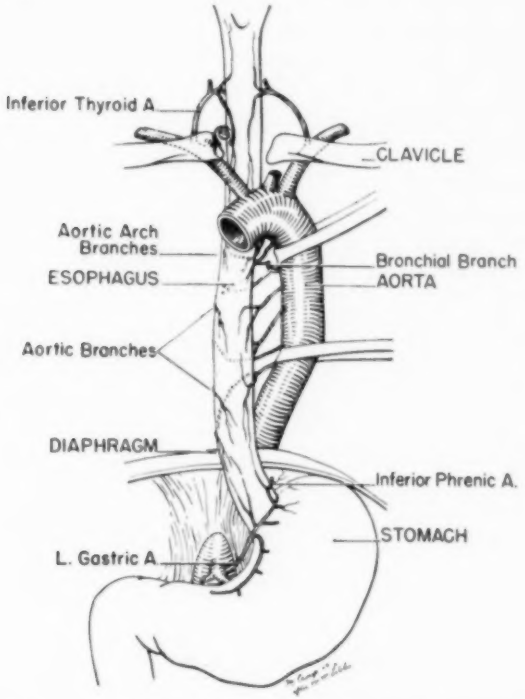


FIGURE 5: Diagrammatic illustration of essential sources of blood supply to the esophagus. The aortic branches, the inferior phrenic artery and the nutrient branches from the inferior thyroid artery are depicted. (Redrawn by M. Croup from M. McLatchie, Sweet, R., Surgery, 1948).

the cardia or at a point along the fundus according to the dictates of the case. The lower end of the esophagus is covered by a rubber glove and the stomach is closed by a two layer continuous inverting suture which may be reinforced by a third row of interrupted sutures (Figure 8).

The stomach is delivered into the thorax and maintained in correct position for anastamosis to the esophagus by means of stay sutures. The esophagus is not divided at the level selected for anastamosis until the esophagogastrostomy has been undertaken, thus permitting the use of the lower esophagus for traction and manipulation during the performance of the anastamosis. It is our custom to employ a three row repair, employing silk throughout (Figure 9). The posterior layer is placed first and is of continuous silk sutures joining the serous surface of the stomach to the muscular wall of the esophagus. Then, the muscular layers of the stomach and of the posterior wall of the esophagus are incised and a second continuous silk suture is begun which unites the posterior portions of the muscular walls of both organs. The mucosa of each organ is then opened and these layers are sutured to each other with a row of interrupted silk. Once the mucosal row has been completed, the esophagus may be entirely divided, and the intermediate muscular row and the outer sero-muscular row are completed.

After the anastomosis has been finished, it is often possible to cover it at least partially by omental tags from the greater curvature of the stomach. Then the stomach is secured by additional

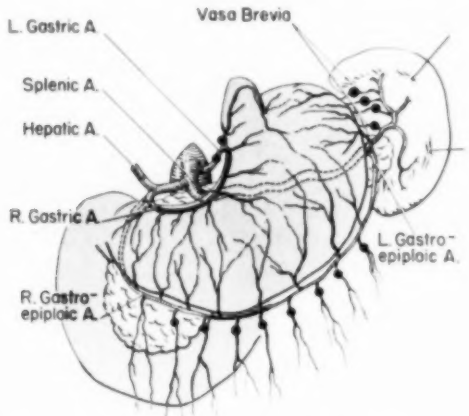


FIGURE 6: Diagram of arterial blood supply of stomach. (Redrawn by M. Croup from M. McLatchie, Sweet, R., Ann. Surg., October 1946).

sutures to the chest wall and mediastinum and the diaphragm is closed (Figure 10) and affixed to the stomach at the margin of the ample opening left for the passage of the organ into the chest. Unless there is evident tension on the stomach and esophagus, we do not crush the left phrenic nerve. An intercostal tube having a large lumen is placed so that the tip is near but not upon the line of anastamosis, to be attached to a water seal drainage bottle. The chest wall is closed in layers after the instillation of 200,000 units of penicillin, divided between the abdominal and thoracic cavities.

Continuity of the gastro-intestinal tract is restored as shown in Figures 11 and 12. In lesions of the gastric cardia or lower esophagus which are considered inoperable, it is often possible to produce a palliative restoration of continuity with ease by means of partial mobilization of the greater curvature of the stomach and delivery of the fundus into the thorax, thereby permitting the preparation of a by-pass above the obstruction by means of a side to side anastamosis of the stomach to the esophagus (Figure 13). Similar shunts between the esophagus and the stomach also can be made at much higher levels and on either the right or left side.

Adequate blood replacement is employed during operation and occasionally supplemented during the postoperative course when needed. Liberal doses of antibiotics are given intramuscularly before and after surgery. Attention is paid to the prompt and complete re-inflation of the lung on the side of operation by

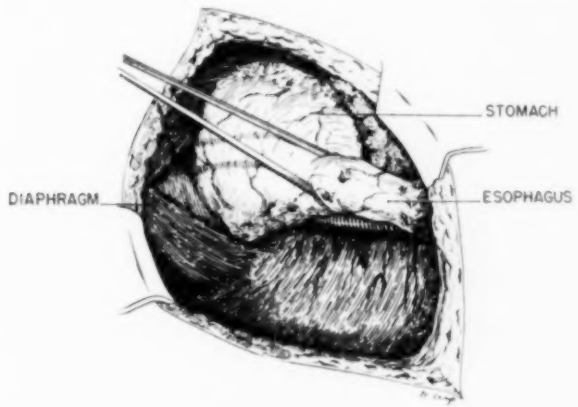


FIGURE 7: Transthoracic resection of lower esophagus or gastric cardia. The lower esophagus has been mobilized, the stomach has been mobilized along both curvatures, and has been delivered into the thorax.

means of the intercostal tube and water seal drain. Alimentation is ordinarily begun cautiously on the third day after surgery and can be advanced steadily thereafter, if no evidence of leak of the anastamosis develops.

Resection of the Esophagus for Carcinoma at or Near the Level of the Aortic Arch

It is quite natural that success in dealing with carcinoma of the lower esophagus would lead to an extension of the application of the technique to lesions arising at a higher level. Garlock[2] and Sweet[3] once more led the way in this direction of surgical progress. The principles of technique remain the same and the stomach is raised to the higher level required to establish continuity. At these higher levels the neoplasm is usually situated at the aortic arch or very close to it. In almost every such instance, it is necessary that the esophagus be mobilized to a point above the aortic arch (Figure 14) and that it then be brought into the

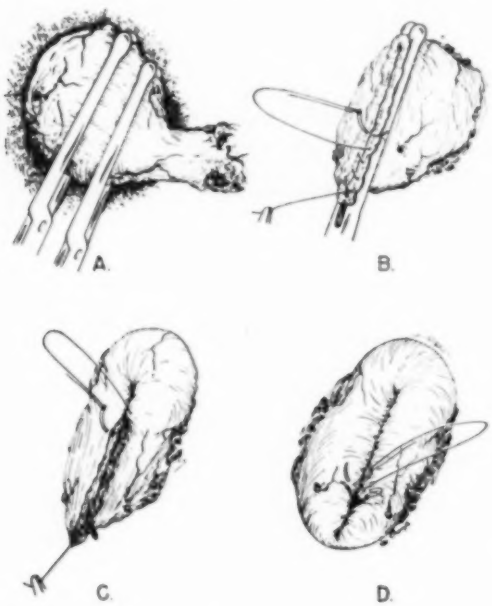


FIGURE 8: (A) Application of clamps across fundus of stomach in preparation for division at this level.—(B) First row of continuous suture employed in closure of stomach.—(C) Second row of continuous suture employed to invert first row after removal of clamp.—(D) Final row of inverting suture of continuous type employed in closing stomach. Similar techniques are used if esophagus is divided at cardia.

left chest over the top of the arch. Division of the esophagus in such instances will be at a point which will usually require the anastamosis to be completed at or above the arch (Figure 15). Very often it is tedious and sometimes very difficult to mobilize the disease bearing portion of the esophagus from the other side of the aorta. Visibility frequently is poor, exposure is often limited, and access for dissection and hemostasis falls short by some measure of being satisfactory. Nevertheless, experience has shown that the operation may be carried out successfully and with excellent end results from a functional stand point (Figure 16). We have found that restoration of continuity by esophagogastrostomy at this level provides very satisfactory deglutition and

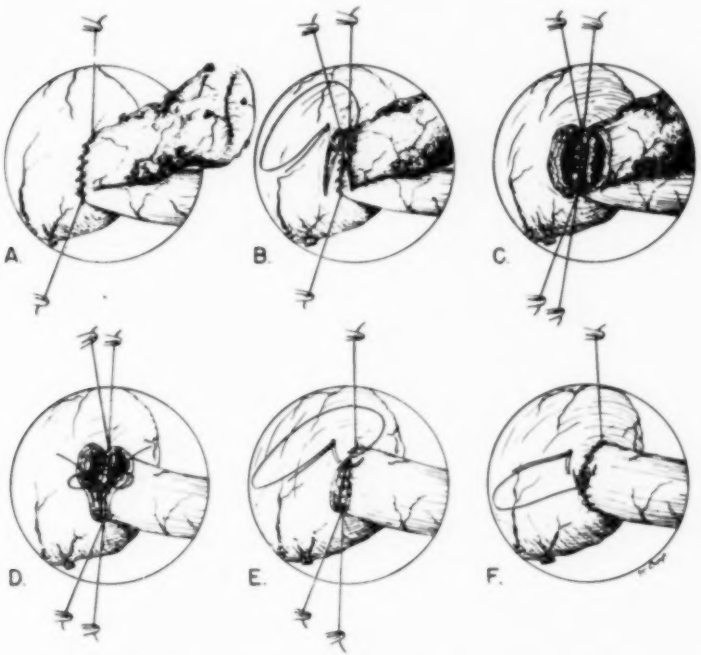


FIGURE 9: Technique of three row anastamosis of esophagus to the stomach: (A) Posterior layer, sero-muscular, continuous, fine silk suture.—(B) Intermediate row, muscular, continuous, fine silk suture. Muscular walls of the stomach and esophagus have been incised and are united to each other by this suture.—(C) Mucosal or internal row of interrupted fine silk sutures. Knots are tied on inside, mucosa of both esophagus and stomach are co-apted with care.—(D) Completion of mucosal row of sutures along anterior aspect of anastamosis.—(E) Completion of muscular or intermediate row of continuous suture from anterior surface of anastamosis.—(F) Completion of the sero-muscular layer around anterior aspect of anastamosis. This suture was the first to be started and is the last to be completed.

very little tendency to regurgitation. The higher the level of the anastamosis the greater are the complications. Accordingly, there is a corresponding increase in mortality rate.

The technical factors differ in some respects in addition to those incurred as a result of dissection to the right of the arch of the aorta from a left thoracic approach. More complete mobilization of the stomach is required in order that it may be raised to the higher point within the thorax, but it invariably can be depended upon to span the gap if properly prepared. More attention is required for preservation of certain structures in the vicinity of the arch, notably the left recurrent laryngeal nerve and the thoracic duct. Furthermore, it is at these levels that the vascular supply of the mid-esophagus will be encountered. As has been shown by Shapiro and Robillard[10] there is considerable variation in precise pattern of the components of the esophageal blood supply. Both anatomical studies and good surgical judgement militate against devascularization of the esophagus farther above the point of anastamosis than is necessary.

Carcinoma of the esophagus which arises in the mid-portion or in the superior thoracic and cervical segments involves the trachea, the carina, and the main bronchi, as the case may be, in the local advance of the neoplasm. Before surgery is undertaken in such

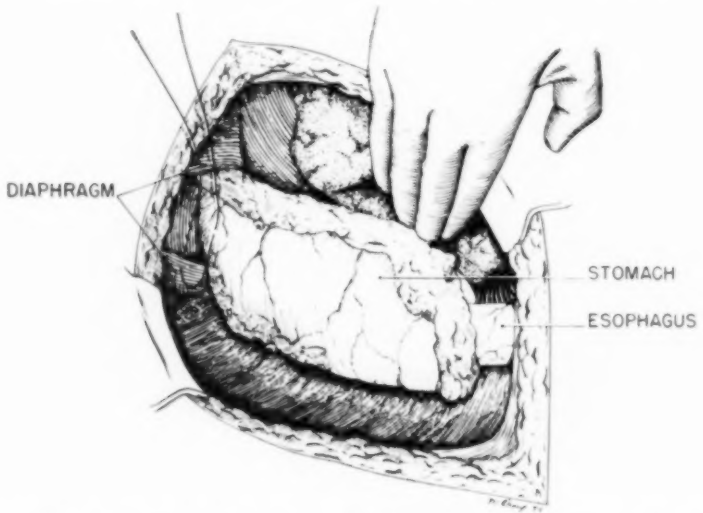


FIGURE 10. The resection of the lower esophagus has been performed and the stomach has been delivered into the thorax where the anastamosis has been completed. The diaphragm is being closed about the stomach. Note that anastamosis line has been partly covered by omentum from the greater curvature.

cases, careful bronchoscopic examination is necessary in order that such complications may be ascertained. Even though such precautions may yield negative endoscopic observations, invasion may be encountered at operation.

The Combined Abdominal and Right Thoracic Approach to Carcinoma of the Middle Esophagus

In 1946, Ivor Lewis of Great Britain[11] published his operation for carcinoma of the mid-third of the esophagus. A two-stage procedure was adopted which included, as the first stage, mobilization of the stomach, exploration of the abdomen, and the making of a jejunostomy. The second stage is performed seven to ten days later and consists of a right thoracic approach to the esophagus by means of a resection of the sixth rib. If the lesion is found operable, the esophagus is mobilized after ligation and division of the azygos vein. The hiatus is enlarged by digital dilatation and the stomach is drawn into the thorax. From this point, the operation proceeds much as has been outlined in the previously discussed left thoracic approach to the esophagus.

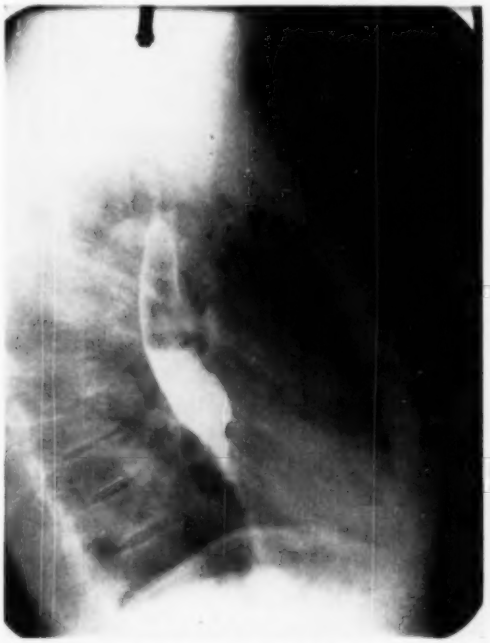


FIGURE 11: Esophagram showing appearance of obstructing carcinoma involving lower third of esophagus.

Lewis believed that this technique offered the following advantages:

1) The abdominal stage provided: (a) a far more satisfactory exploration of the abdomen; and (b) an opportunity to perform a jejunostomy, which is of great value in improving nutrition and hydration between stages and maintaining alimentation in the immediate postoperative period following completion of the second stage.

2) The advantages of the right thoracic approach included: (a) far better access to the upper two-thirds of the thoracic esophagus; (b) only the azygos vein has to be divided to lay bare the entire esophagus; (c) the aortic arch represents a safety barrier to the other pleural cavity, rather than a technical obstacle; and (d) because of the absence of the aortic arch as a detterent, the lesion and the esophagus may be dissected under full vision with excellent exposure.

Macmanus[12] and Kent and Harbison[13] have presented in the literature their experiences with this plan. We have employed Lewis' technique alternately with the left thoracic approach for lesions at and near the arch of the aorta. The technique, as noted above, requires both an abdominal and a thoracic incision. The stomach must be mobilized along the lesser and greater curvatures

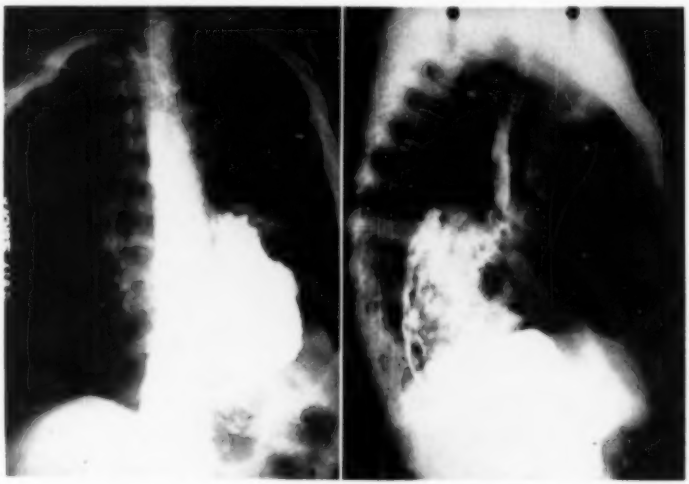


FIGURE 12A FIGURE 12B

Fig. 12. Barium study of stomach after resection of lower esophagus and esophagogastrostomy: (A) Antero-posterior view.—(B) Left Lateral view. The major portion of the stomach has been delivered into the chest and has been anastamosed to the esophagus at a point in the middle third of the structure.

in the same manner as is necessary when the left transthoracic, transdiaphragmatic approach is employed (Figure 17). It has been our experience that this stage is sometimes very tedious and time consuming. Since we have failed to obtain the good results mentioned by Lewis from jejunostomy, that part of the operation has been abandoned by us. Lewis predicted that it would be preferable to perform the two stages at the same time in those patients who were able to undergo such extensive surgery. Again, it has been our experience that both stages should be performed at one time, if at all possible, and currently we are making every endeavor to do so.

We feel that there is no question whatsoever that Lewis' contentions concerning the easier access to the esophagus and the benefits of not having to contend with the aortic arch are valid

FIGURE 13: Esophagram made after palliative by-passing esophago-gastrostomy had been performed. An inoperable carcinoma of the lower esophagus was present. Fundus of stomach was brought through the diaphragm and anastamosed to esophagus at a point above the obstruction. Arrows point to the anastamosis and to the point of complete obstruction at lower end of esophagus.

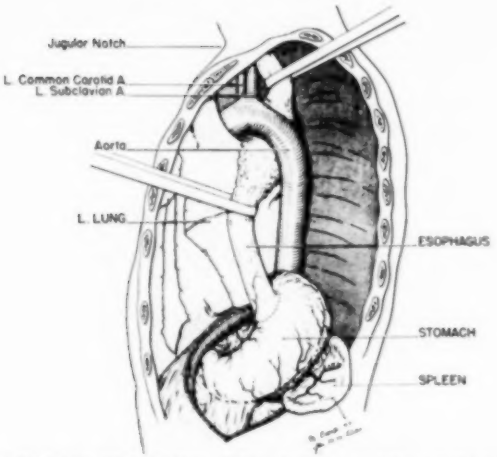


FIGURE 14: Mobilization of the stomach and the esophagus through the left thoracic approach. The lesion is at the level of the aortic arch and the anastamosis will be made above the arch. (Redrawn by M. Croup from M. McLatchie, Sweet, R., Ann. of Surg., October 1946).

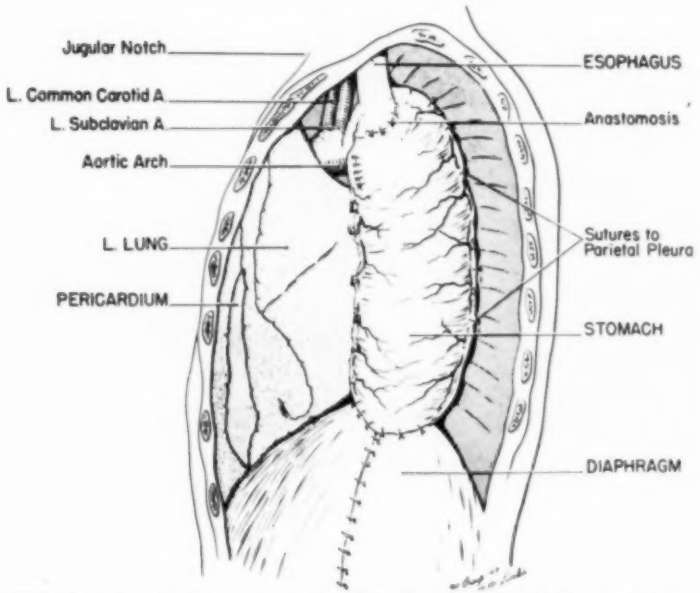


FIGURE 15: Anastamosis above arch of aorta has been completed in left thorax. Note closure of diaphragm and tacking of stomach to parietal pleura. (Redrawn by M. Croup from M. McLatchie, Sweet, R., Ann. of Surg., October 1946).

(Figure 18). The end result of this operation (Figure 19) is exactly comparable with that achieved by the left transthoracic route.

Admittedly, both Sweet and Garlock (13, in discussion) are opposed to the operation advocated by Ivor Lewis. It is our belief that the technical possibilities for the surgical management of carcinoma of the esophagus have not as yet been fully explored and that the operation of Lewis merits widespread trial so that we may evaluate its place in our armamentarium. We have come to no final conclusion for ourselves and perhaps will not be able to do so for years, however, the matter could be settled in a reasonably short period of time if more general investigation of its usefulness were pursued.

Carcinoma of the Upper Thoracic and the Cervical Esophagus

The range of application of the techniques for resection of the esophagus and esophagogastrostomy soon was shown to be almost without limit by both Sweet[14] and Garlock.[15] The entire thoracic esophagus was resected in their cases and the anastamosis of the cervical stump of the esophagus to the stomach was made in the neck. Sweet delivered the esophagus into the neck through the medial aspect of the anterior thoracic cage by resections of anterior portions of the left clavicle and the left first rib while

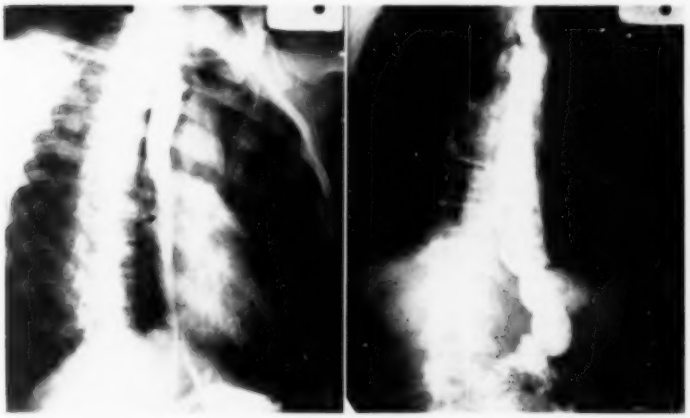


FIGURE 16A FIGURE 16B

Fig. 16: (A) Esophagram demonstrating obstructing lesion of esophagus immediately below level of aortic arch. Biopsy revealed epidermoid carcinoma. (B) X-ray study three weeks after resection of the esophagus and anastomosis of the stomach to the upper esophagus at a point above the aortic arch. The left thoracic approach was employed.

Garlock passed the stomach to the left of the aortic arch and into the neck through the bed of the removed esophagus. In each instance, the anastamosis was performed through a cervical incision which was made parallel to the medial border of the left sternomastoid muscle. Subsequently, similar operations were reported by Wylie and Frazell,[16] Brewer,[17] and Nissen[18] who employed the essentials of the technique of Garlock, and by Scott and Hanlon[19] who also employed Garlock's method in the main.

We have also performed a successful resection of this type of carcinoma of the superior segment of the thoracic esophagus. We employed the procedure outlined by Garlock with excellent results (Figure 20). The cervical incision was made first by us, as is customary, and carotid sheath was retracted laterally while the thyroid was displaced medially. The superior esophagus was mobilized at this time down to the lesion but the carcinoma could

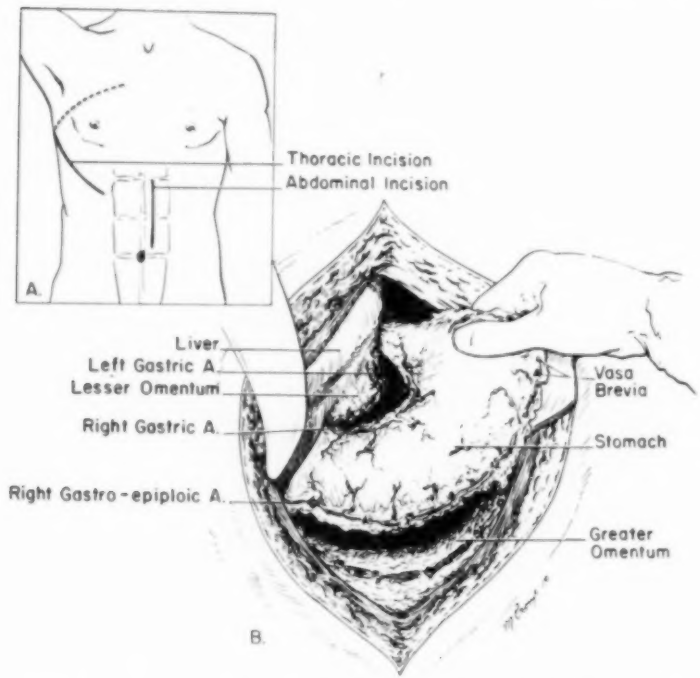
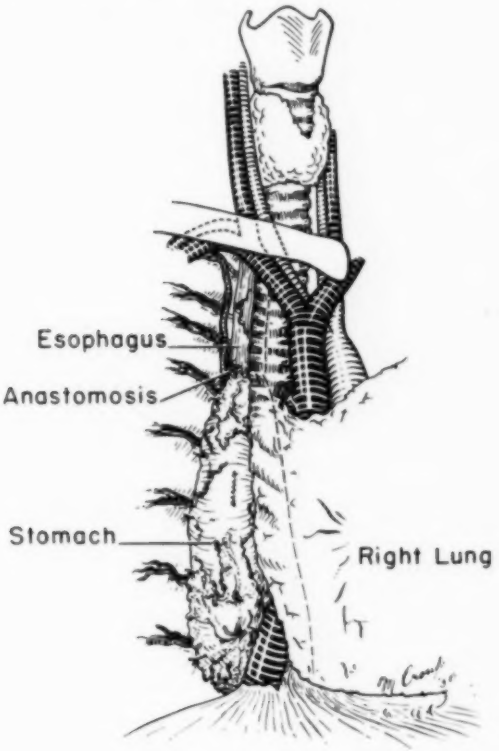


FIGURE 17: Abdominal stage as performed in the combined abdominal and right thoracic approaches. The stomach is mobilized along both curvatures so that it may be delivered into the right thorax. This stage must be carried to completion at this time since adequate access to the abdomen is not available through a right thoracic approach.

not be freed easily along its right border so this move was deferred until the thoracic steps were taken although resectability had been determined.

The thoracic stage was accomplished through an approach made by resection of the left sixth rib. Mobilization of the thoracic esophagus was completed; then the diaphragm was opened and the stomach freed of its attachments to the area of the pylorus, delivered into the thorax, and the lower end of the esophagus divided at its junction with the cardia. The stomach was closed at the cardia and the distal end of the esophagus was covered



C.

FIGURE 18: Drawing of completed second stage through right thoracic approach. Azygos vein has been ligated and divided, esophagus has been mobilized and removed, stomach has been delivered into right thorax and the anastamosis has been completed at level of aortic arch.

with a rubber glove. The entire esophagus was then delivered into the neck and drawn out through the cervical incision. Stay sutures were placed at the highest point on the fundus of the stomach and these were grasped by long hemostats introduced through the cervical incision. The stomach was then passed to the right of the aortic arch and drawn into the cervical wound by a combination of gentle traction on the stay sutures and manipulation from within the thorax. The chest was then closed after installation of a large intercostal catheter for drainage. The patient was turned on his back and the cervical esophagogastrostomy was performed. The functional result (Figure 21) has proven to be very satisfactory.

The postoperative care of patients who have undergone surgery of such magnitude, regardless of the level of the resection, must be managed with meticulous attention to detail. Hydration and alimentation first by parenteral routes and later by mouth, must be thoughtfully carried out. The use of the antibiotics is, of course, mandatory. Efforts to prevent pulmonary complications are vital, and once such complications have begun, aggressive treatment is essential. Prompt re-expansion of the lung on the side of operation should be effected. Loculations of fluid within the pleural space should be watched for, and if discovered, removed by aspiration. The need for blood transfusion during the early postoperative

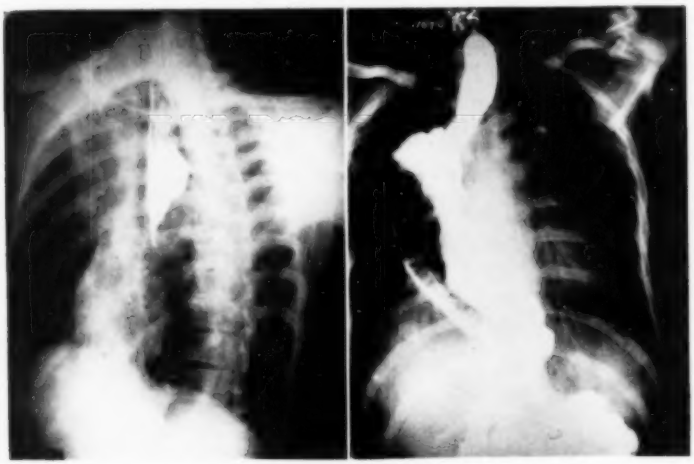


FIGURE 19A FIGURE 19B

Fig. 19.—(A) Esophagram showing marked obstruction at level of aortic arch. Biopsy revealed epidermoid carcinoma of the esophagus.—(B) Resection has been completed employing the combined abdominal and right thoracic approaches. The stomach and esophagus contain barium sulphate and can be seen clearly.

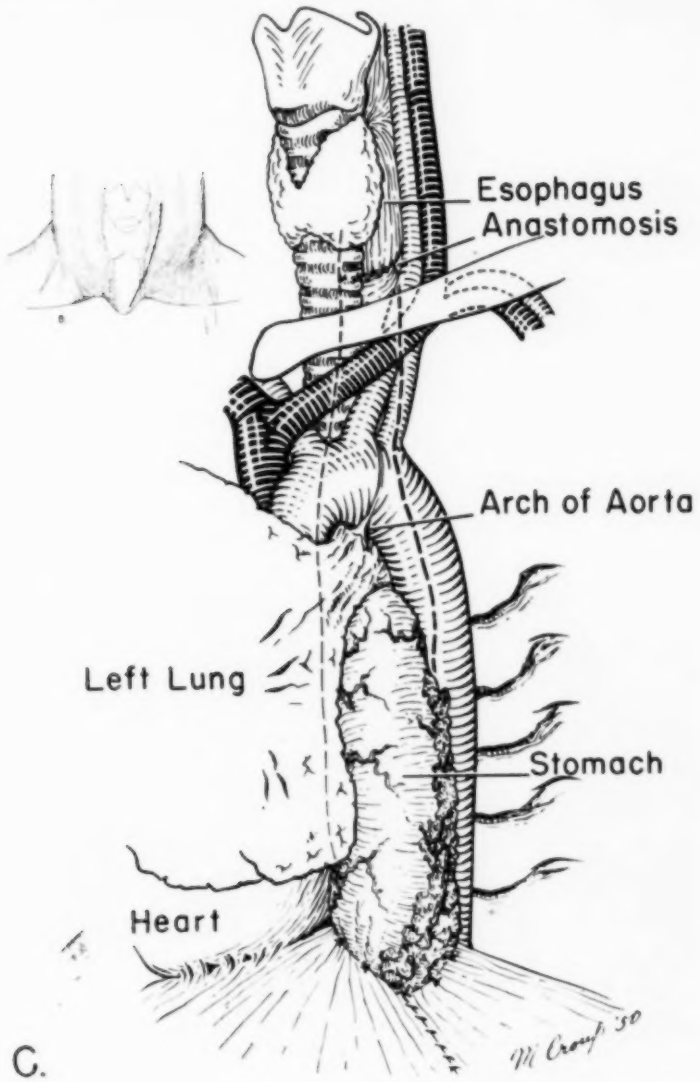


FIGURE 20: Completed esophagogastrostomy in the neck for carcinoma of the superior esophagus. Combined left thoracic and cervical approaches were used as outlined by Garlock. The anastamosis is accomplished through the cervical incision after mobilization of the esophagus and stomach and delivery of both structures into cervical wound.

period should be ascertained by hematological studies. Indeed, surgery of such gravity calls upon all our resources of experience, training, and judgement. Nevertheless, it has been conclusively shown that these procedures are feasible, relatively safe in competent hands, and productive of favorable functional results. As noted above, the highest hurdle before us is the achievement of early diagnosis so that surgery may be made available to the patient before the lesion becomes inoperable and so that five-year survival rate will be enhanced.

A different approach to the surgical treatment of carcinoma of the upper esophagus and of the lower pharynx was conceived by Wookey.[20,21] A local resection through a cervical approach was coupled with a cervical tube graft of skin which bridged the defect between the pharynx and the esophagus, thus restoring continuity of the gastro-intestinal tract.

Bricker, Burford and Eiseman[22] have greatly extended the possibilities of this principle by the use of a previously prepared tubed pedicle graft to bridge the distance between the pharynx and the upper end of the esophagus after resection of the disease bearing upper segment of the organ. A radical neck dissection

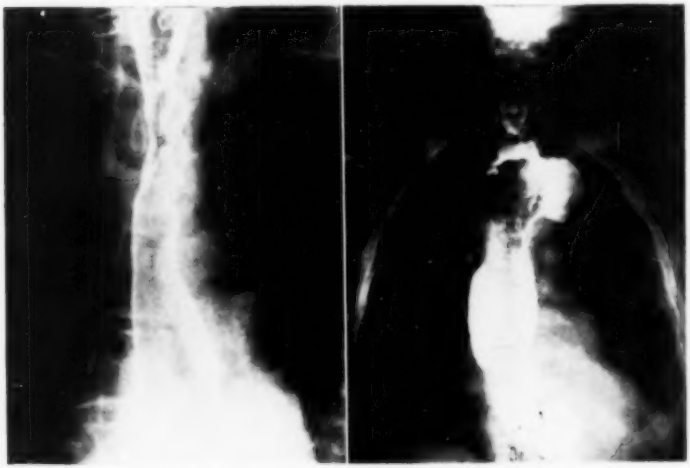


FIGURE 21A FIGURE 21B

Fig. 21: (A) Esophagram reveals irregular obstructing deformity in lumen of esophagus at a level above aortic arch which extends upward to the level of clavicle.—(B) Resection of the esophagus and a cervical esophago-gastrostomy has been performed. The stump of the cervical esophagus, the anastamosis level, and the entire stomach are outlined by barium sulphate. Note that the stomach passes to the right of the aortic arch and that the fundus forms a pouch above the arch.

has been incorporated as part of their technique which is a distinct asset to any plan of surgical treatment for carcinoma in the upper esophagus. Other obvious benefits in this operation are greater scope of usefulness than the Wookey technique and successful application in situations which cannot be dealt with by means of a cervical esophagogastrostomy. Only experience will ascertain whether end results will substantiate the apparent great merit of this contribution to the methods of surgical attack on esophageal cancer. We have had no operative experience with the techniques of Wookey and Bricker, Burford and Eiseman.

SUMMARY

1) Certain milestones on the route of surgical progress in the modern treatment of carcinoma of the esophagus have been enumerated.

2) The techniques of various operative procedures employed in the surgical attack upon this problem have been reviewed briefly.

3) A strong plea has been made that we direct all our efforts toward achieving early diagnosis of carcinoma of the esophagus in order that early treatment may follow.

RESUMEN

1) Se enumeran ciertos jalones en la ruta del progreso quirúrgico en el tratamiento del carcinoma del esófago.

2) Se revisan brevemente los diversos procedimientos quirúrgicos empleados en la lucha quirúrgica contra este problema.

3) Se hace un enérgico llamado a los esfuerzos para lograr el diagnóstico temprano del carcinoma del esófago para obtener un tratamiento inmediato.

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Tumors and Cysts of the Mediastinum

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As a result of developments in thoracic surgery, mediastinal tumors and cysts may no longer be considered merely as pathological curiosities. A large proportion of these lesions may now be cured by resection. For others x-ray therapy provides gratifying palliation. This article is intended as a summary, illustrating some of the more important mediastinal lesions and emphasizing their management. For more exhaustive clinical and pathological discussions of individual mediastinal neoplasms the reader is referred to other papers which have been written on this subject.[1-6]

In surveying the literature, one is impressed by the great variety of tumors and cysts which may be found as primary or secondary lesions of the mediastinum. One also gains the impression that some of these must be extremely rare. While none of them may be considered as particularly common, it seems likely that they occur more frequently than the literature suggests. Now that definitive therapy is available, case reports are appearing more and more frequently.

It is proper to discuss mediastinal tumors and cysts as a group, even though they comprise a large number of lesions that are pathologically unrelated. Significant is the fact that few of the reported cases have been observed in the later decades of life. This would seem to indicate that these lesions, untreated, are generally incompatible with longevity. Since there tends to be great similarity in the clinical manifestations of all of these tumors, one is concerned primarily with differentiating the benign and malignant lesions for which surgery offers some prospect of cure from those for which it is definitely out of the question.

Any tumor or cyst of the mediastinum which is benign at the time of its discovery is considered an operable lesion. Most important among those that may be benign are teratodermoid tumors and cysts, bronchogenic cysts, gastroenterogenous cysts, pericardial coelomic cysts, cystic lymphangiomas, tumors of the thymus, thyroid and parathyroid tumors, neurogenic tumors and the various neoplasms of connective tissue origin. Surgical removal should also be considered for primary, unicentric, malignant tumors of the mediastinum, and for benign lesions which have undergone

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malignant change. All mediastinal neoplasms are considered to be potentially malignant, though malignant degeneration of the cystic types is rare. In addition, there are a few non-neoplastic lesions occurring in the mediastinum which must be considered in a differential diagnosis and for which surgery may be indicated. These include: meningoceles, tuberculomas, echinococcal cysts, mediastinal abscesses, and aneurysms. Lesions for which surgery is not indicated include the lymphoblastomas, Boeck's sarcoid, and secondary malignancies presenting themselves in the mediastinum through metastasis or invasion, though occasionally exploratory thoracotomy may be necessary for diagnosis in this group. Operable and inoperable lesions of the esophagus are not included in this discussion.

Ideally, all mediastinal tumors and cysts would be discovered by routine, periodic chest x-ray films before they had produced symptoms, caused irreparable damage, or undergone malignant change. Through mass x-ray surveys for tuberculosis, routine x-ray examination of military and other personnel, and more widespread realization among practitioners that no examination is complete without at least a fluoroscopy of the chest, more mediastinal lesions are now being discovered at a stage when surgical cure is still attainable.

The first symptoms and signs of mediastinal tumors and cysts are generally attributable to the fact that they displace and compress adjoining structures. Growth is frequently very slow, permitting gradual adjustment to pressure changes. A patient who has harbored a mediastinal neoplasm from birth is often entirely unaware of changes due to pressure until he has reached the third or fourth decade of life, when the growth may have attained tremendous size. An expanding mass in the mediastinum will, in the course of time, manifest itself by producing a sense of fullness or tightness in the chest and eventually pain. The pain may be dull or sharp, localized or widely referred. Pressure on the trachea or bronchi will give rise to a dry, irritative cough. Wheezing may appear as the airway becomes narrowed, and increasing shortness of breath may be noticed. Dyspnea is a common early symptom and sometimes seems to be out of proportion to the size of the mass.

Pressure on a bronchus may result in atelectasis and eventually in bronchopulmonary suppurative disease. Erosion into bronchus or lung may cause hemoptysis or even severe hemorrhage. Cysts rupturing into a bronchus will discharge their contents and are then likely to become secondarily infected. Occasionally infection occurring within a cyst, even without the presence of a bronchial communication, will give rise to the first symptoms of the condition. Complicating bronchopulmonary infection or empyema may

also give rise to toxic symptoms. With malignancy, the usual constitutional manifestations appear: loss of weight and strength, anemia and fever. Vascular compression may manifest itself by dilatation of neck veins, swelling of the neck and face, and development of collateral venous channels over the chest wall. Changes due to nerve involvement are not uncommon in some types of tumor. Lesions involving the paravertebral sympathetic chain are likely to result in inequality of the pupils or in a complete Horner's syndrome. Hoarseness and vocal cord paralysis result from damage to a recurrent laryngeal nerve, and paralysis of a hemidiaphragm occurs when a phrenic nerve is interrupted. Pain in the shoulder, arm, or over the distribution of an intercostal nerve is not uncommon. Compression of the esophagus may produce dysphagia and vomiting of undigested foods. External presentation of a mass or swelling may, under unusual circumstances, be the first evidence of a mediastinal tumor.

Demonstration of a mediastinal tumor or cyst is largely dependent on fluoroscopy or roentgenograms, whether or not there have been significant symptoms and physical findings. The primary concern is then to decide whether or not a surgical cure may be feasible. Additional roentgenographic studies are indicated as a rule and may be very informative. Careful fluoroscopy is important, with attention to demonstrating expansile or transmitted pulsation, movement of the mass with respiration or swallowing, interference with passage of barium through the esophagus, or evidence of diaphragmatic paralysis. In addition to routine posteroanterior and lateral chest films, oblique projections, preferably taken with a barium-filled esophagus, may aid greatly in localizing the mass and determining its relationships. Body section radiograms are also helpful in localization and in demonstrating relationships to important neighboring structures. These simple and innocuous procedures may be sufficient to determine whether or not the lesion is likely to be operable. When x-ray studies demonstrate a well-defined mediastinal mass which is unilateral or predominantly on one side, it is likely to represent a benign type of tumor or cyst which can and should be removed surgically. When a mediastinal mass presents poorly defined borders and when it is equally prominent bilaterally, it is more likely to be a malignant lesion, infiltrating and invading surrounding structures. Multicentric lesions, strongly suggesting malignancy, likewise are considered inoperable.

Careful physical examination is important to search for evidence of primary or metastatic malignancy elsewhere or of complicating disease which might contraindicate surgery. Biopsy of enlarged lymph nodes or other presenting lesions may clinch the diagnosis

and obviate the necessity for more extensive diagnostic studies, including exploratory surgery. In suspected lymphoblastomas of the mediastinum response to x-ray therapy should be evaluated before considering surgery unless a solitary well-defined, unilateral tumefaction is the only lesion evident.

For more exhaustive study of mediastinal lesions a number of additional diagnostic procedures are available, though they are not recommended for routine use. Angiocardiography and venography are primarily of value in differentiating vascular from neoplastic lesions. They may also give valuable information in localizing and delineating nonvascular masses and in demonstrating vascular obstructive phenomena resulting from the latter.[7,8] Bronchoscopy should be used to rule out the presence of a bronchogenic tumor, should this be suspected. Concomitantly, one may gain information in regard to tracheo-bronchial changes from pressure, erosion, or ulceration, and perhaps determine the source of bleeding from the respiratory passages. Bronchography will also demonstrate bronchial obstruction, but is primarily of value when complicating bronchopulmonary suppuration is suspected. Esophagoscopy is indicated only in ruling out the presence of primary esophageal lesions, which are purposely excluded from this discussion.

Roentgenograms following establishment of artificial pneumothorax may occasionally be of diagnostic value in differentiating lesions arising within the lung from other intrathoracic tumors. Thoracoscopy is unlikely to give much information that cannot be obtained radiographically. While transpleural as well as needle or aspiration biopsy of mediastinal tumors is sometimes feasible these procedures are not without hazard and generally are to be condemned. In fact, in the majority of mediastinal lesions, adequate x-ray studies permit the physician to determine whether or not surgery may provide some prospect of cure. This prospect having been established, it appears more reasonable to proceed with exploratory thoracotomy, which at present is associated with very little risk and which simultaneously provides an opportunity for definitive therapy, than to subject the patient to exhaustive diagnostic procedures which themselves are not without some element of risk.

The problem of differential diagnosis resolves itself essentially into determining whether a given tumor is a lymphoblastoma or metastatic malignancy, in which case surgical cure is almost certainly out of the question, or whether it is a benign or malignant primary neoplasm for which surgical cure may be feasible. While in most instances, the advisability of surgery can be determined without establishing the exact nature of the mediastinal

lesion before surgery, we all take justifiable pride in being able to arrive at an exact diagnosis before undertaking surgery, and in reducing to a minimum the number of operations which we must term "exploratory." Clinical manifestations along with x-ray studies make it possible to differentiate a large percentage of mediastinal lesions, 80 per cent according to Curreri and Gale.[3] The location, definition, size, shape and relative density of a roentgenographic shadow, and the demonstration of air, bone, calcification or teeth within its confines are of diagnostic significance. If x-ray films show destructive invasion of bone, this is an indication of malignancy. However, benign tumors, particularly those of nerve origin, may show compressive erosion of adjoining vertebrae, sternum or ribs.

Dividing the mediastinum into anterior, middle and posterior portions, one finds that certain tumors and cysts are more likely to be encountered in each of these zones. In the *anterior mediastinum*, between the sternum in front, the trachea, bronchi, and great vessels behind, and extending upward to the neck, we encounter the teratodermoid tumors and cysts, tumors of the thymus, hyperplastic or adenomatous thyroid and parathyroid glands, and pericardial cysts. The *mid-mediastinum* is the usual site of origin of bronchogenic and gastroenterogenous cysts. Lymphomas and metastatic malignant lesions are also found in this region. In the *posterior mediastinum*, tumors of nerve origin, such as neurofibromas and ganglioneuromas predominate.

It should be remembered that a mediastinal lesion does not necessarily have its origin within the mediastinum. The borders of this region are only relative and a chest wall neoplasm arising along its anterior or posterior border is commonly classified as a mediastinal tumor. Lesions of the neck may encroach upon the superior mediastinum from above. Bronchopulmonary lesions may extend into the mediastinum through the hilum of the lung or by invasion across the mediastinal pleura. The probable extramediastinal origin of such pathology will give a clue as to its nature. The preoperative differential diagnosis of tumors and cysts of the mediastinum is aided by knowledge of their relative frequency and of their age and sex incidence. These and other criteria for clinical differentiation will be developed in discussing separately the various lesions in question.

Among the most interesting lesions of the mediastinum are those resulting from developmental aberrations, particularly the teratodermoid group of tumors and cysts. These are derived from ectoderm and sometimes include elements of mesodermal and endodermal derivation. Other congenital lesions of the mediastinum include: bronchogenic and gastroenterogenous cysts, de-

rived from endoderm and mesoderm; coelomic cysts, derived from mesoderm; and cystic lymphagiomas derived from mesoderm.

1. *Teratodermoid tumors and cysts.*[9,10]

It has been common practice to separate this group into the more solid and complex teratomas and the epidermoid and dermoid cysts, but there is very little practical or pathological justification for subdividing them thus. The more cystic tumors of the group have a more uniform, rounded appearance by x-ray, while the more solid types present greater variation in density, more irregular borders, and are more likely to be malignant or to develop malignant change. However, developmentally, clinically, and pathologically it is proper to classify them together.

The vast majority of intrathoracic teratodermoid tumors originate in the anterior mediastinum, directly behind the sternum and in front of the pericardium and great vessels (Figs. 1 and 2). Rarely they are found in other locations (Fig. 3). Roentgenographic

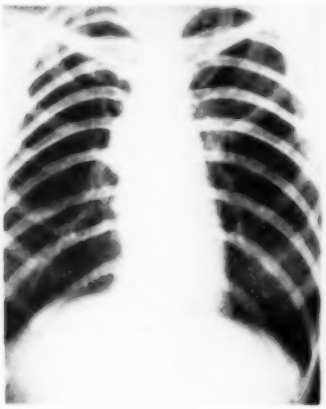

FIGURE 1

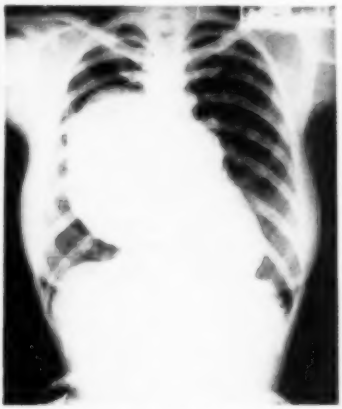

FIGURE 2

Fig. 1: E.L.; white, female; age 35; November 1946. Fatigue, chest pain and dyspnea for 14 years. Swelling to right of mid-sternum appeared in 1933, aspirated several times. X-ray therapy in 1935, 1945 and 1946, when pain became more severe. Thoracotomy May 20, 1947. Resection of substernal mediastinal cyst with calcification in its wall. Pathologic diagnosis: "Dermoid cyst of the mediastinum." Symptoms relieved.

Fig. 2: M.V.N.; white, female, age 39; July 1946. At 23 years had severe pains in neck, left shoulder and around heart. Treated with bed rest, digitalis, and aspirin. Increasing shortness of breath. Thoracotomy October 10, 1946. Removal of large mediastinal cyst from right hemithorax with extension into left hemithorax. Portions of cyst wall very thin and densely adherent to great vessels and pericardium. During surgery severe cardiac arrhythmia developed but normal rhythm returned. Pathologic diagnosis, "Cystic mediastinal teratoma, benign."

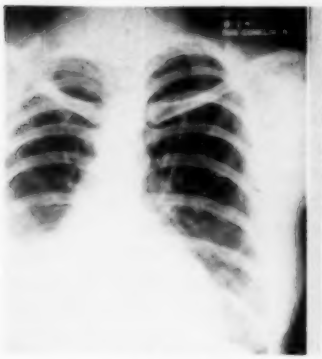

FIGURE 3A

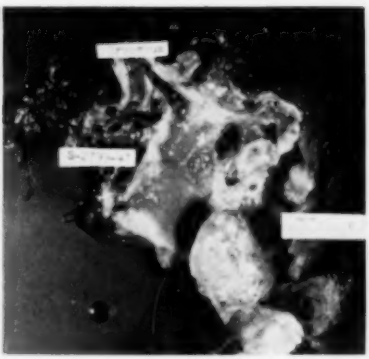

FIGURE 3B

Fig. 3: F.W.; white, female; age 35; March 1947. Empyema drained on right in 1933, followed by persistent productive cough. Pneumonia, right, in 1945. Recurrent hemoptysis between 1933 and 1945. Sputum negative for tubercle bacilli. Appendectomy in February 1947, because of recurrent aching in right chest and abdomen. Thoracotomy August 5, 1947. Resection of cyst with attached basal segments of right lower lobe. Pathologic diagnosis, "Dermoid cyst with communication to a bronchus; bronchiectasis, atelectasis." Complete relief of symptoms. Following surgery and on specific questioning, patient recalled that she had coughed up hairs occasionally over a period of several years.

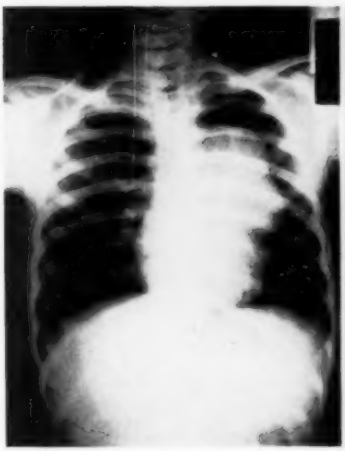

FIGURE 4A

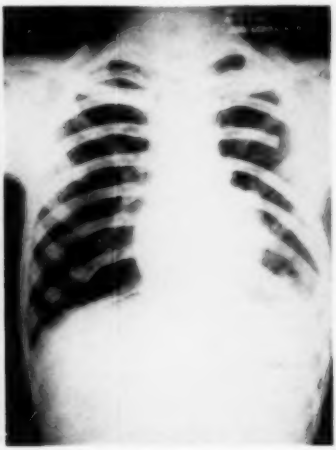

FIGURE 4B

Fig. 4: G.B.; white, male; age 14; March 1947. No symptoms referable to chest. Mediastinal tumor found during course of physical examination. Thoracotomy April 3, 1947. Large mediastinal tumor removed. Numerous pleural implants found. Pathologic diagnosis, "Malignant teratoma of mediastinum." Patient died June 14, 1947.

evidence of calcification within the wall of a teratodermoid cyst is frequent, while tooth and bone formation within a mediastinal tumor is diagnostically specific. Air and a fluid level may be demonstrated within such a cyst which has ruptured into a bronchus. Since their growth tends to be very slow, unless infection or malignant degeneration supervenes, pressure symptoms generally do not become evident until the second, third, or fourth decade of life. Unless removed, these tumors nearly always cause death before the fifth decade. In about 15 per cent of reported cases, the lesion was malignant at the time of diagnosis, malignancy accounting for fatality in almost all of these (Fig. 4). Infection and complications due to pressure phenomena are the usual causes of death in the remainder.

The contents of a teratodermoid cyst may become infected spontaneously, presumably by a hematogenous route, whereupon the cyst is likely to increase rapidly in size. Pressure as well as toxic symptoms become prominent and rupture into a pleural cavity or a bronchus may prove rapidly fatal. More often infection is secondary to rupture of the cyst into a bronchus with development of a bronchocystic fistula. Such rupture may manifest itself by expectoration of sebaceous material, cholesterol crystals, and hair, an event pathognomonic of this condition. Strangely enough, cysts with bronchial communication may exist for years undiagnosed. The signs and symptoms of chronic bronchopulmonary suppuration may or may not be present. A history of expectoration of hair may be elicited only through specific questioning and the diagnosis may not be established prior to surgical intervention (Fig. 3). Unusual cases have been reported by Maier[11] and Gebauer.[12]

Extirpation provides the only satisfactory management of teratodermoid tumors and cysts. Roentgen therapy is of no value. Improvement by marsupialization and drainage has been reported and conceivably such preliminary management may be indicated in patients so ill that they are unlikely to tolerate more radical surgery. Eventual extirpation, if feasible, would still be recommended.

2. *Bronchogenic cysts.*[5,13,14]

These cysts are considered to arise through pinching off of a bud of the foregut in the embryo. Most frequently they arise in the middle portion of the mediastinum in relation to the trachea or major bronchi (Fig. 5). Similar cysts whose walls are also lined with ciliated columnar epithelium like that of the respiratory tract, are found in relation to the esophagus (Fig. 6). An unusual location for such a cyst is illustrated (Fig. 7). The characteristic

lining may be partially or completely destroyed as a result of pressure atrophy from accumulation of mucus secreted by glands in their walls. Cartilage and smooth muscle may also be found in the walls of these cysts.

Symptoms, if any, are generally due to pressure on trachea, bronchus, or esophagus, producing shortness of breath, cough, or dysphagia. Rarely such a cyst communicates with the trachea or a bronchus,[13] in which case the contents are likely to become infected and there will be expectoration of purulent sputum, which is sometimes bloody. The presence of air or a fluid level may then be demonstrable within the cyst by x-ray. Otherwise, the typical roentgenographic appearance is that of a smooth rounded mass having the density of fluid.

Generally these cysts cannot be differentiated clinically from other lesions of the mediastinum and their removal is indicated for diagnosis and for relief of symptoms. Hardy[14] found that 82 had been reported in the literature, and added a case in a ten-month infant in which the cyst was successfully removed. Including his case, 54 of the 83 patients were treated surgically and 50 recovered. Hardy's case and a nine-month old infant reported

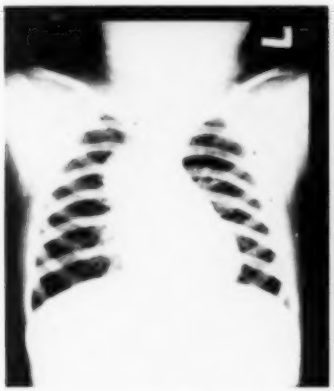

FIGURE 5

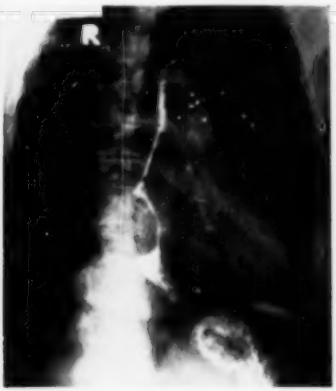

FIGURE 6

Fig. 5: T.W.; white, female; age 5; June 1949. Unexplained fever, maximum 106 degrees F., for one month. Mediastinal mass found on routine fluoroscopy. Thoracotomy June 21, 1949. Resection of mediastinal cyst from between superior vena cava and trachea. Pathologic diagnosis, "Multilocular ciliated columnar epithelial cyst of the mediastinum."

Fig. 6: V.S.; white, female; age 64; November 1946. Dysphagia, nausea, vomiting beginning October 16, 1946. Barium trickled past rounded mass in lower one-third of esophagus. Esophagoscopy November 8, 1946, negative. Thoracotomy November 12, 1946. Pathologic diagnosis: "Esophageal cyst probably representing aberrant respiratory tract with chronic inflammation." The cyst was beneath muscular coat of esophagus. Symptoms relieved.

by Maier[15] were the only operated cases under the age of 18 (Figs. 5 and 8).

3. *Gastro-enterogenous cysts.*[16,17,18]

Among the rarer cysts of the mediastinum are those with linings resembling gastric or enteric mucosa. Bickford[16] recently reported the 24th case of true gastric cyst. Pressure symptoms and pain are likely to occur, particularly if there is functional secretory activity of the lining. Peptic ulcer with perforation has been reported. Cysts containing both alimentary and respiratory tract elements are reviewed by Cassel, et al.,[19] reporting resection of such a cyst in a 24 year old man. Ladd and Scott[20] report recovery in three patients treated by marsupialization of the cyst followed by destruction of its mucosal lining. The treatment of choice, however, is total excision.

4. *Pericardial coelomic cysts.*[21,22]

Thin-walled cysts lying close to the pericardium and lined with mesothelial cells have been classified by Lambert[22] as pericardial coelomic cysts. He attributes development of these cysts to failure

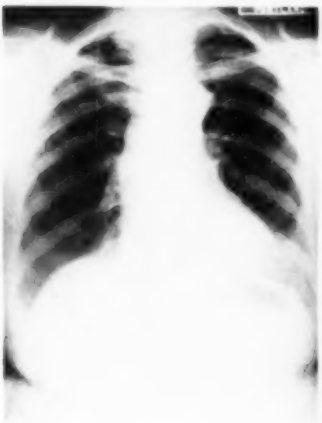

FIGURE 7

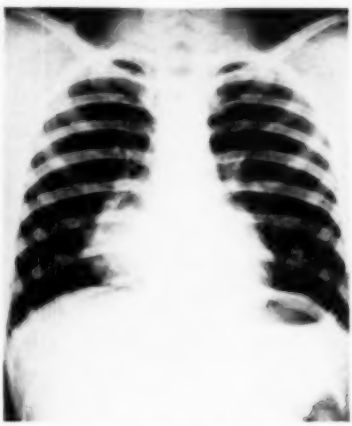

FIGURE 8

Fig. 7: A.P.; white, female; age 63; August 1948. No symptoms referable to the chest. Small rounded density at right apex found on routine chest film. Thoracotomy September 9, 1948. Resection of small cyst in posterior mediastinum. Pathologic diagnosis, "Cyst, apparently of respiratory tract origin."

Fig. 8: N.L.; white, female; age 6; April 1948. Density in right lower chest discovered fluoroscopically at one year of age. Gradual increase in size. Asymptomatic. Thoracotomy May 10, 1948. Resection of mediastinal cyst from between middle and lower lobe with pedunculated extension running upward between inferior and superior pulmonary veins into the mid-mediastinum. Pathologic diagnosis, "Bronchogenic cyst."

of one of the primitive pericardial lacunae, appearing early in embryonic life, to merge with the remainder in the formation of the pericardium. As a result an independent cavity or cyst appears. Since the lining cells are difficult to distinguish from vascular endothelium, it may be impossible to differentiate these histologically from so-called cystic "hygromas" or lymphangiomas. The cyst cavity is filled with a clear fluid which has given rise to the term "spring water cyst."

Pericardial coelomic cysts are generally asymptomatic, though there may be vague distress or cough due to pressure. They are generally discovered on a routine roentgenogram of the chest, and appear as a rounded, well-defined mass of "fluid" density. Removal is readily accomplished, and is indicated in order to prevent complications from pressure phenomena and because these lesions cannot be differentiated clinically from those with a more serious prognosis (Fig. 9).

5. *Lymphangiomas.*[23,24]

Cystic lymphangioma or "cystic hygroma" occurs with relative frequency in the neck. Rarely it is found in the mediastinum, in which case it is generally associated with cystic hygroma of the neck. While these cysts cannot be differentiated histologically from pericardial coelomic cysts the latter are unilocular and are

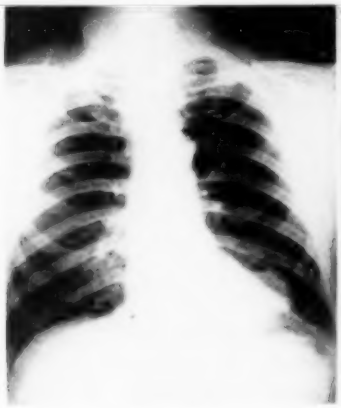

FIGURE 9

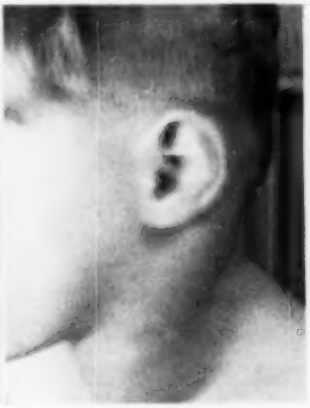

FIGURE 10A

Fig. 9: R.W.; white, male; age 59; April 1949. Recent pulmonary hemorrhage. At thoracotomy April 28, 1949, rounded density at left heart border proved to be blood-filled cyst with bronchial communication. Coelomic cyst "?".

Fig. 10A: J.R.; white, male; age 3; March 1949. Photograph showing fluctuant swelling (cystic hygroma), in child's neck. See Figures 10B and 10C.

generally found in the neighborhood of the pericardium, usually near the diaphragm. On the other hand, cystic lymphangiomas are multilocular and present themselves in the superior portion of the anterior mediastinum. In 1931, Lemon[23] reported two cases of cystic hygroma, cervical and mediastinal, in children. One of these cases, followed for two years, showed no response to x-ray therapy. The other died and at necropsy was found to have partial atelectasis of both lungs and pressure on the heart. Sanes, et al.[24] reported removal of a cystic lymphangioma from the mediastinum of a 59 year old man and cited the few cases reported in American and foreign literature. Extirpation is indicated to relieve or prevent pressure phenomena (Fig. 10).

6. *Thymic tumors.*[25,26,6]

(a) *Benign tumors of the thymus.*

Benign thymoma is a rare tumor of the mediastinum. By x-ray study it generally appears as a flattened density in the superior anterior mediastinum directly behind the sternum. Whether discovered on a routine roentgenogram or as a result of pressure symptoms, resection is indicated as with all benign mediastinal tumors.

Particular interest has been aroused by thymic lesions because hyperplasia of the thymus or benign thymoma has been found in a significant number of patients suffering from myasthenia gravis. Since the original report of Blalock[25] a number of patients with

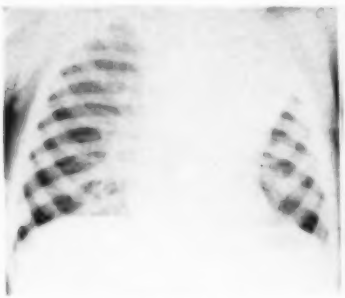

FIGURE 10B

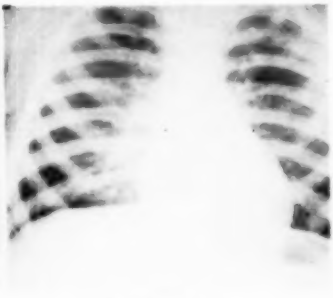

FIGURE 10C

Fig. 10. J.R.; white, male; age 3; March 1949. Neck swelling, first noted at one month, suddenly increased in size in February 1949, from behind left ear to trachea and clavicle anteriorly. Frequent respiratory infections with persistent rattling cough. Bilocular cyst and lymph nodes removed from neck March 14, 1949. Pathologic diagnosis, "Cystic hygroma of neck, chronic lymph adenitis of cervical lymph node." Thoracotomy April 13, 1949. Resection of large multilocular mediastinal cyst, cupola to left hilum, surrounding phrenic and vagus nerves. Pathologic diagnosis, "Mediastinal cystic hygroma, thymic tissue, cystic hygroma of pleural surface."

myasthenia gravis have been treated by thymectomy. Thompson[6] collected 52 cases so treated. Variable benefit had been reported in 28, little or no benefit in 9. There were 11 deaths, no follow-up on 4. In most cases of myasthenia gravis subjected to surgery an actual tumor of the thymus has not been demonstrable.[26] The value of thymectomy in myasthenia gravis is not yet well established.

(b) *Malignant tumors of the thymus.*

Lymphosarcoma, carcinoma, Hodgkin's disease, and teratoid tumors are described as originating in the thymus gland. These lesions are often difficult to classify, for it may be impossible to determine whether they are primary in the thymus or elsewhere. Well-defined solitary tumors which may be of thymic origin should be removed, if possible. Those that are inoperable should be treated with roentgenray therapy. While malignant thymomas are stated to be radioresistant they cannot be differentiated from lesions which are known to be radiosensitive until roentgenray therapy has been given a trial.

7. *Mediastinal thyroid.*[27,6]

Adenomas of the thyroid, particularly those occurring at the lower poles, will occasionally descend gradually into the anterior

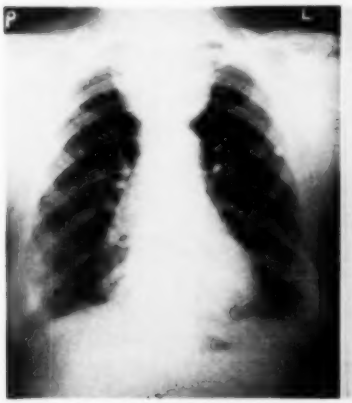

FIGURE 11

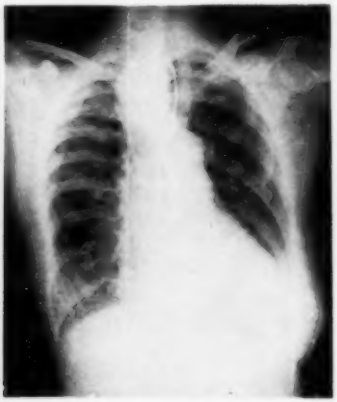

FIGURE 12

Fig. 11: S.J.; white, female; age 61; July 25, 1949. Chest pain one year, increasing dyspnea, occasional wheeze. On fluoroscopy mass in anterior superior mediastinum moved upward on swallowing. Trachea in mid-line, esophagus deviated to right. Resection August 11, 1949 through split sternum. Pathologic diagnosis, "Nodular adenomatous hyperplasia of thyroid." Symptoms relieved.

Fig. 12: C.G.; white, female; age 60; April 1946. Posterior mediastinal mass displacing esophagus anteriorly and to left. Thoracotomy May 7, 1946. Pathologic diagnosis, "Adenomatous hyperplasia of the thyroid with marked degeneration, including hyalinization and calcification."

mediastinum, following the line of least resistance as they grow, encouraged by the negative pressure within the thorax, by gravity, and by swallowing and respiratory movements. Mediastinal or substernal thyroid is seen most often in women past middle age. Dyspnea, cough and dysphagia from compression of the trachea and esophagus are the usual manifestations. Mild toxicity with exophthalmos may be associated. A mass is generally palpable in the suprasternal notch, particularly on swallowing and coughing, and the trachea may be shifted to one side.

Widening of the superior mediastinal shadow in the postero-anterior roentgenogram is characteristic. By fluoroscopy the mass is seen to move with swallowing or cough. Resection is generally indicated and can usually be carried out through the neck.[27] For larger mediastinal tumors of the thyroid splitting of the superior portion of the sternum may be required for adequate exposure (Fig. 11).

According to Sweet[28] intrathoracic goiters that lie in the posterior mediastinum always have a pedicle-like connection with the thyroid in the neck. Goiters in this location are rare and diagnosis can be established only following their removal (Fig. 12). A few intrathoracic goiters will show malignant change.

8. *Mediastinal parathyroid adenomas.*

Cope, in 1941, reported 58 parathyroid adenomas in 54 patients.[29] Of these 11 were found in the anterior mediastinum and 5 in the

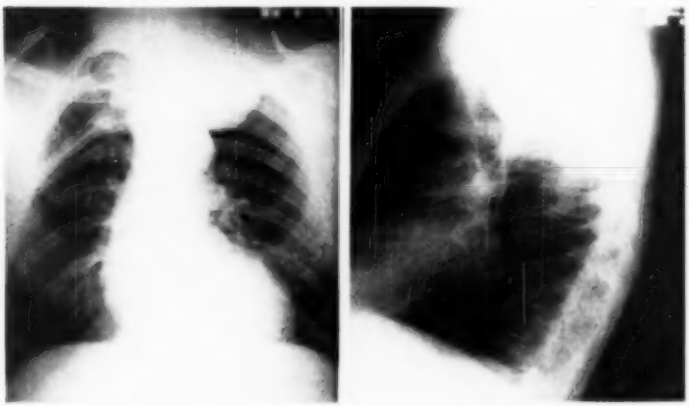

FIGURE 13A FIGURE 13B

Fig. 13. F.E.; white, male; age 49; January 1948. Chest tumor found in 1945, on survey film. Progressive enlargement under observation. No symptoms except "nervousness." Thoracotomy March 11, 1948. Resection of neurogenic tumor from posterior mediastinum. Pathologic diagnosis, "Neurofibroma."

posterior mediastinum, the remainder in the neck. In hyperparathyroidism, when careful search has failed to reveal one or more adenomas in the neck, the mediastinum should be thoroughly explored, since about one out of every four parathyroid tumors will be found in this region. These tumors are rarely large enough to be demonstrable by x-ray.

9. *Neurogenic tumors.*[30]

These are the tumors which are most frequently encountered in the posterior mediastinum, usually in the superior portion of the thorax. Frequently these tumors are discovered on routine x-ray of the chest, in which case they may be entirely asymptomatic. Pain with intercostal nerve distribution is, however, characteristic of mediastinal neurofibroma, and Horner's syndrome is not uncommon, particularly with ganglioneuromas. Hour-glass extension through an intervertebral foramen may occur, producing the signs and symptoms of an extra-medullary spinal cord tumor.

Roentgenographically these tumors present rounded, sometimes lobulated, sharply defined homogeneous shadows (Figs. 13 and 14). Rib or vertebral erosion or widening of an intervertebral foramen is likely to occur and to be evident by x-ray.

A high percentage of these tumors is malignant or will develop malignant change (37 per cent according to Kent, et al.[30]). X-ray therapy is considered of no value and early complete excision is always indicated (Fig. 15).

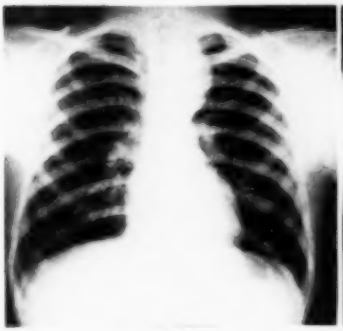

FIGURE 14

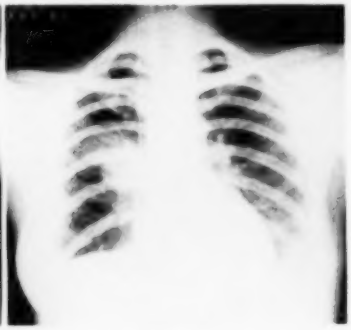

FIGURE 15

Fig. 14: D.F.; white, male; age 16. Mediastinal ganglioneuroma.

Fig. 15: J.K.; white, female; age 29; September 1946. Pain in right lower chest anteriorly since 1944. Fatigue and twelve pound weight loss, two years. Tumor removed from posterior mediastinum January 2, 1947. Pathologic diagnosis, "Neurogenic sarcoma." Last seen August 1, 1949. No evidence of recurrence. (Seen again in March 1950, when a well-defined, rounded 5 cm. mass was found on routine x-ray in the anterior mediastinum at the cardiohepatic angle. Pathologic diagnosis following resection was: "Neurogenic sarcoma." No other metastases could be demonstrated.)

10. *Pheochromocytoma.*

Maier's case[31] was the third intrathoracic pheochromocytoma to be reported in the literature. X-ray evidence of a mediastinal mass, in a patient with hypertension which can be lowered transiently by adrenolytic drugs, should lead one to suspect a mediastinal pheochromocytoma.

11. *Glomus tumor.*

Glomus is a rare benign tumor usually found in the extremities.

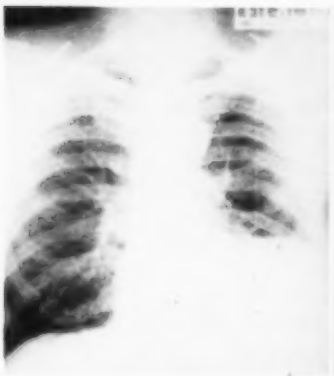

FIGURE 16A

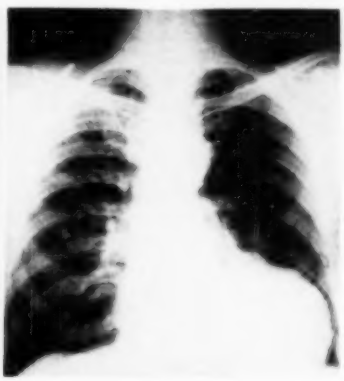

FIGURE 16B

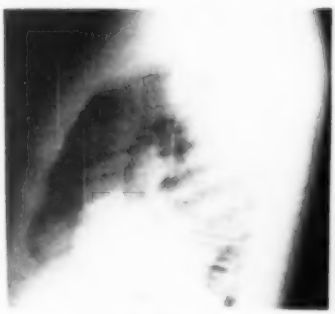

FIGURE 16C

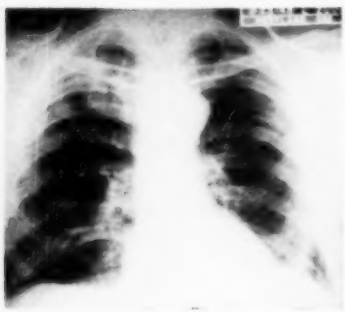

FIGURE 16D

Fig. 16: W.K.; white, male; age 64; September 1947. No symptoms referable to chest. *Fig. 16A:* PA chest film. December 16, 1947. *Figs 16B* and 16C: PA and lateral chest films. October 7, 1947, following artificial pneumothorax. Bronchoscopy September 20, 1947, showed narrowing of left lower lobe bronchus by bulging of posterior wall (extrinsic pressure). Biopsy negative. Thoracotomy October 9, 1947. Resection of large tumor with pedicle, approximately 10 cm. long, originating in anterior mediastinum at level of aortic arch. Pathologic diagnosis, "Pedunculated mediastinal fibroma." *Fig. 16D:* Chest film, November 12, 1948.

Brindley[32] has reported its occurrence in the mediastinum. The outstanding symptom is pain.

12. *Connective tissue tumors.*

These include fibromas, lipomas,[33,34] xanthomas,[35] chondromas, etc., with their malignant counterparts. Usually they are slow in growth and they may attain huge size (particularly the lipomas)[36] before symptoms become manifest. Symptoms, when present, are generally those of compression. Hour-glass extension into the spinal canal or through an intercostal space may occur. These tumors cannot be differentiated clinically. Whether benign or malignant, they are not amenable to x-ray treatment. Removal is always indicated when feasible (Figs. 16 and 17).

13. *Metastatic malignancy.*

Metastatic sarcoma is rare in the mediastinum, deposits being more likely to occur in the lungs. Metastatic carcinoma occurs quite frequently in the mediastinum. The primary source is usually a bronchogenic carcinoma; but the esophagus and breast are also

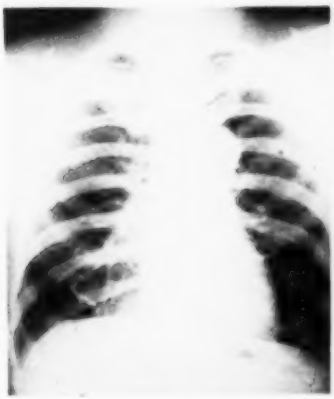

FIGURE 17

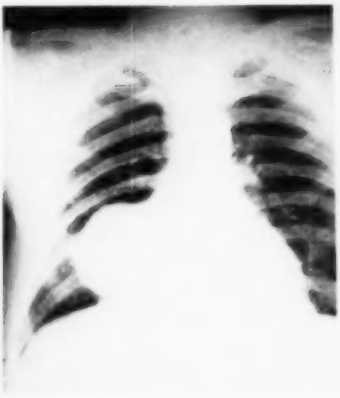

FIGURE 18

Fig. 17. R.M.; white, male; age 43; March 1946. Asymptomatic. Thoracotomy April 11, 1946. Resection of neoplasm from sixth vertebra and rib. Pathologic diagnosis, "Chondroma of rib, possibility of sarcoma." August 1949, no evidence of recurrence.

Fig. 18. C.K.; white, male; age 65; November 1946. Mass "big as a large walnut" found by x-ray in 1936. Slight morning cough for years, hemoptysis three times, recurrent attacks of malaise, fatigue, headache, muscle soreness, chills and fevers (103 to 104 degrees F.), loss of twenty pounds in six months. Mediastinal tumor removed November 22, 1946. Pathologic diagnosis, "Benign tumor, largely lymphomatous." Febrile attacks have recurred less frequently, remain unexplained.

fairly frequent sources. Metastatic chorionepithelioma has also been reported in the mediastinum.[37]

Metastases in the mediastinum are usually multiple and their discovery is, as a rule, an incidental finding in the study of patients in whom primary malignancy has been demonstrated elsewhere. Rarely a mediastinal metastasis might manifest itself before the primary neoplasm can be discovered or suspected. In such a case exploratory surgery and attempted resection may seem advisable. Otherwise, symptomatic treatment only is available. A trial of x-ray therapy may be recommended in an effort to relieve pain and other pressure symptoms. In chorionepithelioma stilbesterol therapy would be indicated.

14. *Superior sulcus tumors.*

These tumors, associated with the Pancoast syndrome, are generally considered to arise within the lung, though they may invade the mediastinum as may carcinoma in other parts of the lung. Roentgenographically these tumors sometimes cannot be differentiated from primary tumors arising in the superior mediastinum. No surgical cures have been reported. X-ray therapy is sometimes recommended in an attempt to relieve pain from bone and nerve involvement.

15. *Primary lymph node tumors.*

(a) *Benign lymphoma.*

This tumor is certainly rare, if it occurs at all, since pathologists question the existence of such an entity. I have not found a report of benign lymphoma of the mediastinum in the literature, but have removed a mediastinal tumor which was "largely lymphomatous" and evidently benign (Fig. 18).

(b) *Lymphosarcoma.*[38]

This is generally a rapidly progressive and fatal disease. When primary in the mediastinum the tumor usually grows with rapidity and eventually fills the entire mediastinum, surrounding and compressing the great vessels, bronchi and other structures. Pressure symptoms become extreme, eventually leading to exhaustion or asphyxia. Diagnosis may be difficult during the early stages of the disease, unless an involved peripheral lymph node is available for biopsy. Splenomegaly may be demonstrable and hematologic studies, including sternal marrow biopsy, may give diagnostic information.

Lymphosarcoma is one of the most common malignancies of the mediastinum and the diagnosis should be suspected when

there is bilateral widening of the anterior and middle mediastinum by a tumor with irregular or lobulated borders. In suspected cases a therapeutic test with x-ray (750 r to 1500 r) is indicated. Surgical exploration may be undertaken in those which are not radiosensitive when the diagnosis remains unconfirmed or when there seems to be some prospect of total resection.

Rarely a mediastinal lymphosarcoma presents itself as a unilateral circumscribed mass, simulating one of the benign tumors or cysts that have been discussed above. Resection without preliminary trial of irradiation therapy is justified in such a case.

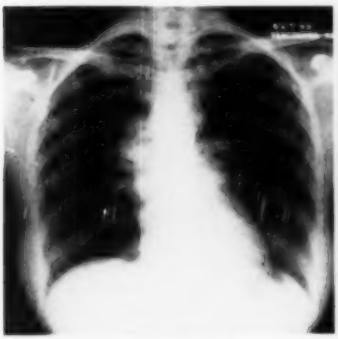

FIGURE 19A

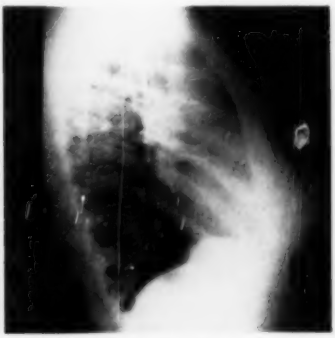

FIGURE 19B

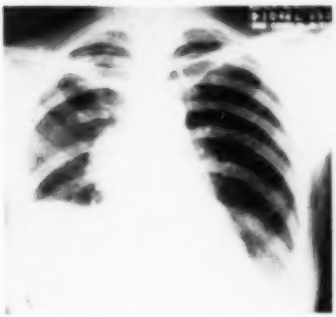

FIGURE 19C

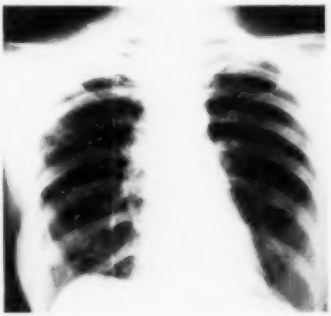

FIGURE 19D

Fig. 19: F.B., white, female; age 35; July 1948. Slight nonproductive cough, easy fatigue and slight exertional dyspnea since April 1948. *Figs. 19A and 19B:* PA and lateral chest films July 1948. Bronchoscopic impression: Neoplasm producing extrinsic pressure on right main stem bronchus. Invasive mass found at thoracotomy August 31, 1948, anterior to hilum in right midmediastinum. Biopsy report, "Malignant lymphoblastoma of uncertain type, but resembling so-called reticulum form." *Fig. 19C:* Chest film September 10, 1948, following exploratory thoracotomy. *Fig. 19D:* Chest film July 8, 1949, ten months following irradiation therapy.

whether or not the diagnosis is suspected. Survival of over five years without evidence of recurrence has been reported[39] (Figs. 20 and 21).

(c) *Hodgkin's disease.*[40]

Mediastinal involvement occurs in about 50 per cent of cases of Hodgkin's disease, this being only one manifestation of the

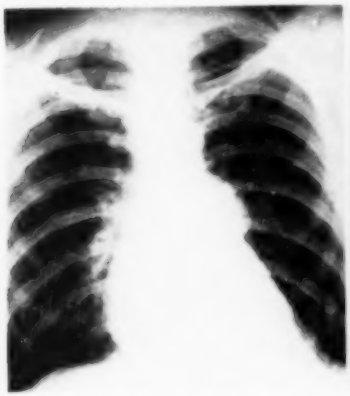

FIGURE 20A

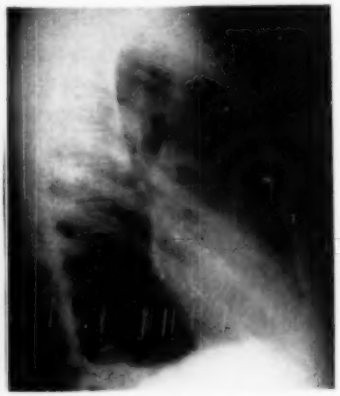

FIGURE 20B

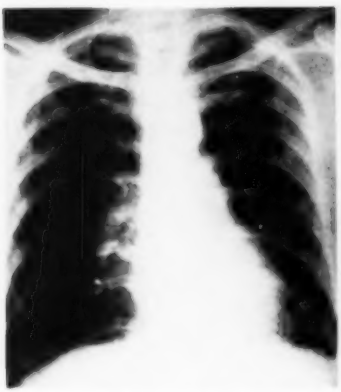

FIGURE 20C

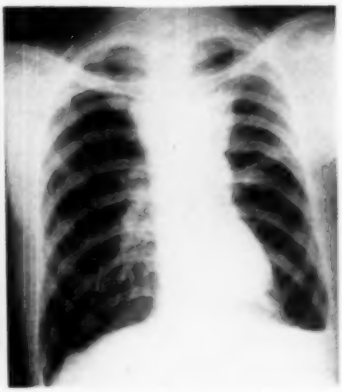

FIGURE 20D

Fig. 20: W.M.; white, male; age 52; October 1944. Fever of 104 degrees F. and pain under left clavicle beginning September 1944. *Figs. 20A and 20B:* PA and lateral chest films October 9, 1944. Thoracotomy October 26, 1944. Well circumscribed tumor resected. Pathologic diagnosis, "Lymphosarcoma of mediastinum, possibly originating in thymus." *Fig. 20C:* Postoperative chest film February 2, 1945. *Fig. 20D:* October 17, 1949, recurrence had been apparent since early in 1949. No response to irradiation therapy; however, patient still clinically well and working.

malady. The symptoms and xray findings in these cases are similar to those in lymphosarcomas of the mediastinum, but peripheral nodes are usually available for diagnostic biopsy. The mediastinal mass will often melt away rapidly with roentgenray therapy. Marked symptomatic relief and gratifying palliation may thus be achieved. Nitrogen mustard ("methylbis") has been used with variable success in cases which are initially or eventually radioresistant and in patients with such widespread involvement that even "spray radiation" therapy is not practicable (Fig. 22).

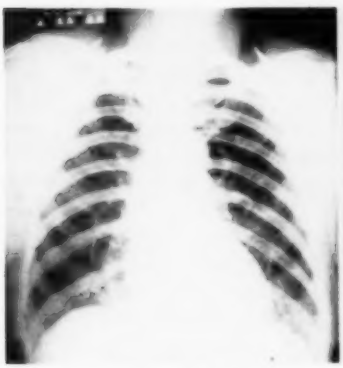

FIGURE 21A

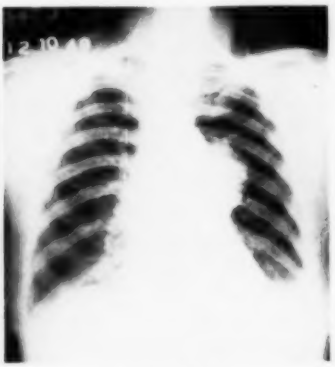

FIGURE 21B

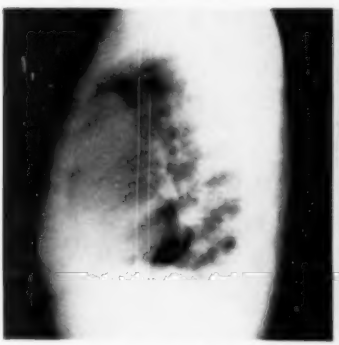

FIGURE 21C

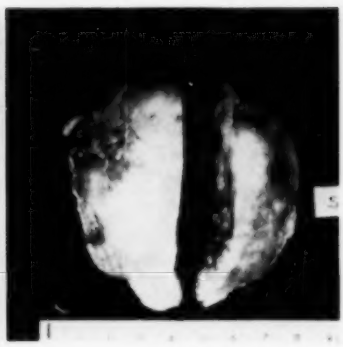

FIGURE 21D

Fig. 21: A.S.; white, female; age 58; December 1949. Cough for six years, wheeze for five years, and chest pains for one year. Chest pain more severe in December 1949, and associated with fever. *Fig. 21A:* Chest film March 11, 1946. Small rounded bulge below aortic knob apparently not noted. *Fig. 21B and 21C:* PA and lateral chest films December 10, 1949. Patient referred to radiologist who recommended resection without preliminary test course of x-ray therapy. Thoracotomy with resection of mediastinal tumor on December 20, 1949. *Fig. 21D:* Photograph of gross specimen. Pathologic diagnosis, "Lymphosarcoma of the mediastinum."

Occasionally the mediastinum seems to be the primary site of Hodgkin's disease, presenting the picture of a solitary benign mediastinal tumor. If such a lesion actually has a unicentric origin, surgical cure should be possible. There is at least some evidence that surgical removal, followed by irradiation therapy, offers a better prognosis than x-ray treatment alone.[39]

16. *Miscellaneous.*

In the differential diagnosis of mediastinal tumors and cysts one must keep in mind mediastinal and paravertebral *abscesses* and infectious granulomas such as *tuberculomas.*[41,42] *Sarcoidosis* with mediastinal lymphadenopathy may simulate Hodgkin's disease and exploratory thoracotomy has been performed for diagnosis. Mediastinal tumefaction may also be evident in *leukemia.* *Echinococcal cysts* may simulate the cysts discussed above. Occurrence in the mediastinum is rare, as compared to the lung. The diagnosis is suggested when a mediastinal cyst is associated with liver involvement and eosinophilia. The presence of echinococcus infestation may be confirmed by the Casoni reaction. Perforation into lung and bronchus may occur, in which case scolices and daughter cysts may be expectorated and a fluid level in the cyst may be demonstrated by x-ray. Echinococcal cysts in the posterior mediastinum with hour-glass extensions into the spinal canal have

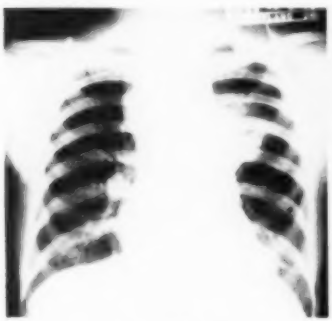

FIGURE 22

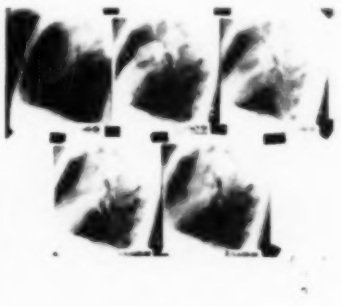

FIGURE 23

Fig. 22: D.C.; white, female; age 36; July 1948. Pain and swelling of neck noticed March 1948. Dysphagia, hoarseness, dyspnea and coughing spells since May 1948, loss of seventeen pounds. Neck mass explored April 1948. Biopsy diagnosis: "Acute and subacute inflammation." Had persistent draining sinuses in neck when first seen. Biopsy of axillary lymph node and neck sinus July 31, 1948. Pathologic diagnosis, "Hodgkin's disease involving axillary lymph nodes with focal, acute, suppurative inflammation; subacute inflammation in vicinity of draining ulcer of left side of neck." Patient treated with methylbis, no significant response. Died February 5, 1949.

Fig. 23: D.H.; white, male; age 45. Angiocardiograms. Aneurysm of aorta compressing left pulmonary artery. Diagnosis established at surgery.

been described. *Meningoceles* may present themselves in the thorax, simulating mediastinal neoplasms. Exploratory surgery determines the diagnosis and surgical cures have been reported.[43]

Aneurysms of the aorta or one of its branches may sometimes present a diagnostic problem, particularly if expansile pulsation of the mass cannot be demonstrated fluoroscopically. Even angiograms with diodrast may fail to confirm the diagnosis, since the dye will not enter a clotted aneurysm (Fig. 23). On the other hand aortic pulsations may be transmitted to a mediastinal tumor mass, causing it to erode through the sternum or ribs. Such a pulsating tumor may simulate an arterial aneurysm.[44]

Report of Cases

Space does not permit a detailed review of personal cases. For statistical purposes, however, it may be desirable to place on record the mediastinal tumors and cysts which we have explored or resected, since none of these have been reported previously. In a total of 29 cases are included the following: *Teratodermoid tumors and cysts*, 5, including one with bronchocystic fistula and one malignant teratoma; *bronchogenic cysts*, 4, including one esophageal; *pericardial coelomic cysts*, 2; *cystic lymphangioma*, 1; *substernal thyroid*, 1; *ectopic thyroid*, 1; *neurofibroma*, 3; *neurogenic sarcoma*, 1; *ganglioneuroma*, 2; *fibroma*, 1; *chondroma*, 1; *liposarcoma*, 1; *metastatic (?) malignancy*, 1; *benign "lymphomatous" tumor*, 1; *lymphosarcoma*, 4.

Of the 29 operations performed 3 were exploratory only, including the liposarcoma, the metastatic (?) carcinoma and one lymphosarcoma. In one lymphosarcoma, multiple mediastinal and hilar masses were resected in order to relieve pressure symptoms but without prospect of cure. This patient died a few months later from progression of his disease. The patients with liposarcoma and metastatic (?) malignancy are presumed to be dead. The only other known death is a 14 year old boy, who had a malignant teratoma, death occurring ten weeks after surgery. There were no deaths attributable to surgery and there were no significant surgical complications.

CONCLUSIONS

Practically all mediastinal tumors and cysts, as well as the lesions with which they may be confused, threaten the life of the patient. During their growth they may compress vital organs, rupture, become infected, or develop malignant change. The most important consideration in these lesions is to differentiate those which are amenable to surgical attack, particularly benign tumors and cysts and primary malignancies, from those for which surg-

ical cure is impossible. A preliminary trial of roentgenray therapy is recommended for known or suspected lymphoblastomas. In these it may provide palliation as well as diagnostic information.

Exploratory thoracotomy is now a relatively safe procedure which may be recommended with impunity for lesions which are potentially malignant or from which fatal complications are likely to ensue. In most mediastinal lesions the diagnosis may be suspected, but cannot be verified, prior to surgery. Thoracotomy should be performed without delay in all cases for which there is some prospect of surgical cure.

CONCLUSIONES

Prácticamente, todos los tumores del mediastino y los quistes del mismo así como las lesiones que con ellos pueden confundirse, amenazan la vida del enfermo. Durante su crecimiento pueden comprimir órganos vitales, pueden romperse, infectarse o tornarse malignos.

Lo más importante de estas lesiones es diferenciar las que pueden tratarse quirúrgicamente, especialmente los tumores benignos y los quistes así como los tumores primarios malignos, de aquellos cuyo tratamiento quirúrgico es imposible. Se recomienda un ensayo preliminar de la roentgenterapia para los limfoblastomas conocidos o sospechados. En estos puede ese ensayo dar información diagnóstica o ser paliativa.

La toracotomía exploradora es ahora relativamente segura y es un procedimiento que puede ser recomendado con impunidad para las lesiones potencialmente malignas o para aquellas que pueden tener complicaciones fatales. En la mayoría de las lesiones mediastínicas el diagnóstico puede sospecharse, pero no puede comprobarse sin la cirugía. La toracotomía debe llevarse a cabo sin dilación en todos los casos en que hay una posibilidad de curación quirúrgica.

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Tumors of the Chest Wall

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Denver, Colorado

Tumors of the chest wall, though relatively uncommon, comprise an interesting chapter in thoracic disease. Medical literature contains numerous single case reports which indicate as great a variance of neoplastic processes as may occur elsewhere in the body. The diagnosis of tumor is relatively easy in most instances but the treatment often taxes the ingenuity of the surgeon. However, the broadening scope of thoracic surgery and newer methods of closing large defects in the chest wall are now bringing to surgery many cases that were previously considered outside the realm of operability.

In spite of their relative infrequency, tumors of the chest wall comprise a large and heterogeneous group which is not amenable to classification. However, they can, for purposes of discussion, be separated into secondary and primary growths.

Secondary Growths

Perhaps the most common tumors of the chest wall are metastatic growths arising from some close or distant primary source. An example of this is the unfortunately common finding of subcutaneous nodules in or near the scar of a previous radical mastectomy. Metastatic growths very frequently involve the parietal pleura and rib structure of the thoracic cage. Here their multiplicity usually simplifies the diagnosis, but occasionally an isolated single metastatic lesion poses a great diagnostic problem.

Before proceeding to a discussion of primary growths, mention should also be made of a group of conditions which might simulate tumor. Actinomycosis thoracis (Fig. 1) may first manifest itself by a swelling on the chest wall much in the same way that empyema necessitatis comes to the surface. A tuberculous abscess may slowly and painlessly arise on the chest wall when the primary lesion lies within the thoracic cage or within a thoracic vertebra. Herniation of the lung resulting from a chest wall defect of traumatic or surgical origin should not be confused with chest tumor.

Primary Growths

For clinical purposes, primary chest wall neoplastic processes are best classified by their tissue of origin. Such tumors may

arise from the skin or its component parts, from the connective or supporting tissue and from the nervous or vascular system supplying the chest wall.

Tumors of the Skin and Subcutaneous Tissue

Benign epidermoid tumors such as sebaceous cysts may and frequently do arise in the skin of the chest wall. However, these and other benign tumors such as papillomata have no characteristics that distinguish them from their counterparts on other parts of the body. However, because of the rather large skin area involved, congenital lesions such as hemangiomas, pigmented moles, etc., may be or may become very large. For the most part, the skin of the chest wall is relatively thick, particularly over the back, the subcutaneous tissue is loose and the blood supply generous. These factors facilitate plastic procedures and materially ease the work of the surgeon in his attack on large cutaneous

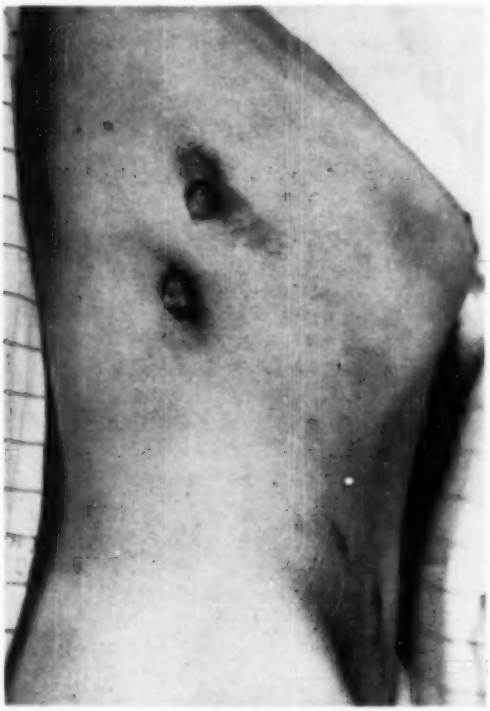

FIGURE 1: Actinomycosis of chest wall secondary to subphrenic abscess.

lesions. By the same token, malignant skin lesions may be widely excised and the resulting defects closed without presenting too great a plastic problem.

Tumors arising within the subcutaneous tissue most frequently are benign lipomas and multiple neurofibromas. Nothing more need be added to the discussions of lipomas, for they have the same characteristics here as elsewhere. However, in the case of neurofibroma the thoracic surgeon is greatly concerned, particularly with their multiplicity. In a case of an intrathoracic neurofibroma, a thorough search of the entire body should be made for other manifestations of the same neoplastic process. Von Recklinghausen's disease, neurofibromatosis, very frequently involves the tissues of the chest wall.

Case 1. One of us was recently asked to examine an 18-year old boy with typical symptoms of an expanding intracranial lesion. One discrete subcutaneous nodule was found in the left lateral chest wall, biopsy of which revealed it to be a typical neurofibroma. This information was a great aid to the neurosurgeon in his diagnosis and approach to a typical neurofibroma of the eighth nerve.

One further note on tumors arising within the subcutaneous area is tissue reaction to foreign body. Foreign material, especially metallic, may reside in the chest wall for long periods. Fibrous tissue may gradually build up around such a body and give rise to a "tumor-like mass." Stemmerman and Duffy[1] recently reported a case of a "true" tumor or cyst lined with bronchial epithelium surrounding a metallic object, shrapnel, which had apparently passed through lung tissue carrying with it basal epithelial elements of a bronchus and coming to lie subcutaneously without connection to the deeper structures.

Tumors of the Connective Tissue

Benign tumors of muscle or fibrous tissue are relatively rare. Isolated cases, fibromas, myomas, rhabdomyomas, etc., may occur but undoubtedly are infrequent. Much more common are their malignant counterparts, the sarcomas. Usually of the fibrosarcoma type with a predominance of spindle cells, they may assume varying grades of malignancy. They may have their origin in the superficial tissues or the deeper structures lying external to the rib cage. They are usually comparatively large when first encountered by the surgeon and present a difficult surgical problem. Wide excision is the only definitive treatment, for roentgen-ray therapy cannot be relied upon.

Primary Tumors of the Ribs

Primary tumors of the ribs are perhaps not as uncommon as might be expected. Each surgeon interested in thoracic disease

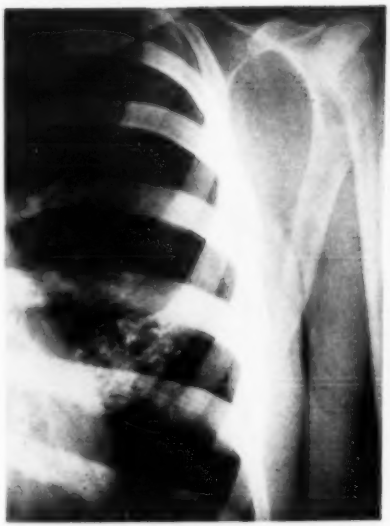

FIGURE 2

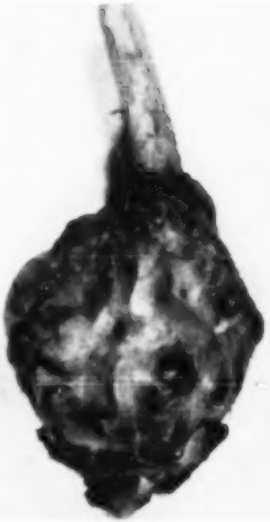

FIGURE 3

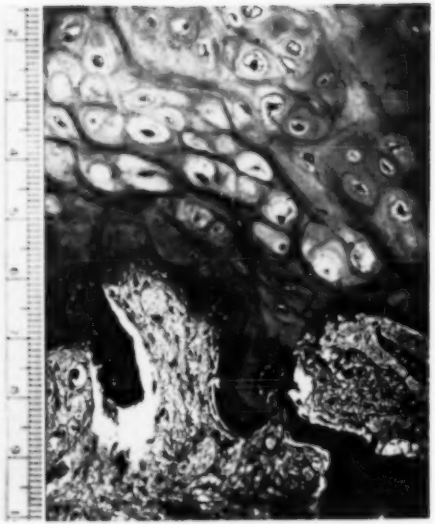

FIGURE 4

Figure 2: Roentgenogram of enchondroma of rib and cartilege.

Figure 3: Gross specimen of enchondroma of rib.

Figure 4: Photomicrograph of sectional enchondroma showing cartilege, bone and myxomatous tissue.

probably has a small series which he has not reported, but which, in their aggregate, would demonstrate that they were relatively frequent. Many tumors in this classification are very benign, their growth may continue for many years and may gradually extend inwardly to displace pulmonary tissue and give rise to no symptoms or objective signs. It is very likely that many such tumors are never called to the attention of the physician. In a recent mass chest x-ray survey in this locality when over 325,000 individuals were x-rayed, approximately 10 cases were discovered which were interpreted as primary rib tumors, hitherto unknown.[2] This survey was carried out primarily for intrapulmonary tuberculosis and no definitive diagnosis was completed on these cases. This figure, therefore, represents only the impression gained from examination of the x-ray films.

The most common of the benign tumors of the ribs are the large group of chondromas. These may be made up entirely of cartilagenous elements, but osseous and myxomatous elements may also be present in varying degrees giving rise to designations of myxochondroma, osteochondroma, etc. These terms merely represent different stages of the same pathologic process. They might arise in long bones from cartilagenous nests and are sometimes referred to as enchondromas or ecchondromas. Most frequently they are anteriorly placed near the costochondral junction. In 1939, one of us collected some 60 cases of this type of tumor.[3]

As stressed by Hedbloom[4] as early as 1921, such benign tumors are prone to recur if not completely removed, since incomplete removal apparently stimulates the growth of the remaining tissue. In a personal series which one of us followed for over one year, 5 of 11 cases recurred. Geschickter and Copeland[5] made the observation that chondromas of the chest wall when associated with chondromas of small bones of the hands showed a greater tendency to recur after removal than those in which only one rib was involved.

Whether such tumors undergo malignant degeneration or whether malignant elements are within them from their start would create argument among pathologists. Graham[6] pointed out that many of these tumors which seem grossly benign recur after removal and even form metastasis. Because of this observation for practical clinical purposes, he considers cartilagenous tumors of the chest wall as malignant from their start. Hedbloom,[7] Roberts[8] and others have emphasized this tendency to malignant change. Boyd[9] mentions sarcomatous degeneration but adds the same thought of whether such a tumor was not malignant from the beginning. Nevertheless, the chance of such tumors being or becoming malignant is so great that there should be no com-

placency about them in the minds of surgeons. Wide and immediate removal is the only treatment. There should be no assumption of benignancy on the basis of x-ray or clinical characteristics. Most authorities feel that such tumors do not respond well to irradiation.

At the present time, treatment of such chondromas resolves itself into the technical problems of their removal. It may be necessary to remove such large sections of the ribs, pleura and diaphragm that repairing the defect, while still leaving a fairly stable thoracic cage, is difficult. Janes'[10] method of swinging a rib diagonally across the defect with its periosteum and underlying vessels intact is a very ingeneous method and has been used with various modifications.

Case 2: M.W., a 17 year old girl, was first seen in April 1938. She gave a history of having had a "lump in her left breast" for about one year. She said that the lump had been increasing in size during the preceding two months. There was no history of trauma, and she did not complain of pain, dyspnoea or tachycardia. Her past history was essentially negative. The patient was a well-developed and well-nournished young girl. On examination, a hard nodular, fixed tumor was felt behind the left breast almost directly behind the nipple. It apparently arose from the 4th rib. The tumor was not tender to palpation. The breast and lungs were normal on examination. Roentgenograms of the chest revealed a multilocular tumor approximately 5 cm. in diameter involving the anterior end of the 4th rib on the left side (Fig. 2). The tumor, together with a section of the rib, was removed through an anterolateral incision extending around the breast. The patient's convalescence was uneventful. Examination of the tissue showed a tumor encircling a rib and its costochondral junction (Fig. 3). It was of cartilagenous consistency with border nodular areas. Microscopic examination showed the tumor to be made up chiefly of cartilage (Fig. 4). There were a few small areas of bone and an occasional small area of fibrous tissue. The patient has been followed for eleven years. There has been no recurrence.

Primary Malignant Tumors of the Ribs

Chondrosarcomas and chondromyxosarcomas arise in the same locations as their more sedate brothers, the chondromas. As mentioned above, the gradation between a benign and malignant chondroma is a gradual one and often even the microscopic picture cannot define the true status. Suffice it to say that highly malignant sarcomas arising from cartilage and bone of the ribs have not been reported frequently. Janes[10] was able to collect six individual case reports. The majority of these patients developed early metastasis. The prognosis even after radical resection is poor.

Case 3: The patient was a white female, aged 60 years. She was first seen in 1941. She complained of dyspnea and pain in the right side of the chest. She gave a history of having fallen and broken several ribs on the right side of her chest in 1916. Following this injury she had persis-

tent pain in the right side of her chest anteriorly for many months, but it finally disappeared. In 1931 she again began to notice a pain in her chest so that she would have to lie down at times to relieve it. In 1935 she first noticed a lump in the region of the sternum. It was not tender but steadily increased in size. In 1938 she began to notice that she was more dyspneic, and at about that time she developed coughing spells when she would lie down or bend over. There was no sputum. Her appetite was good, and she had no nausea. Her only complaint referable to her gastro-intestinal tract was frequent eructations of gas. On examination the patient was found to be well developed and well nourished. She weighed 175 pounds and considered that to be her normal weight. Her blood pressure was 190 120. Her pulse was 80 per minute, temperature was 98.2 degrees F. Examination of the chest revealed a tumor mass in the region of the seventh and eighth costochondral junctions which protruded very little above the normal contour of the chest wall. However, the tumor was felt to extend into the abdomen and occupied almost the entire upper abdomen as far down as the level of the umbilicus. The anterior chest wall was dull to percussion as high as the third intercostal space. There were no other significant abnormalities. Roentgenograms of the chest showed a huge, clearly circumscribed tumor which almost filled the right side of the chest. Films of the abdomen showed that this tumor extended into the abdomen and occupied almost the entire upper part of the abdomen (Fig. 5). The operation was performed under intratracheal anesthesia with cyclopropane. The incision was started just below the sternal notch, and following the midline of the sternum it was continued in the rectus sheath of the abdomen to the level of the umbilicus. The abdominal incision was deepened so that the abdominal part of the tumor could be explored. It was found to occupy almost the entire upper part of the abdomen, having displaced the liver, stomach and other

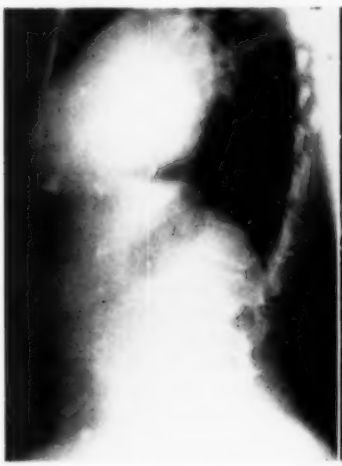

FIGURE 5

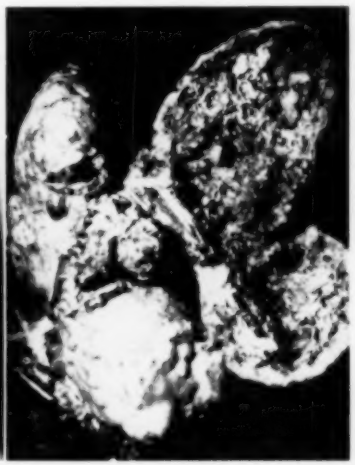

FIGURE 6

Figure 5: Roentgenogram of huge myxochondrosarcoma occupying both chest and abdomen.—*Figure 6:* Cut specimen of myxochondrosarcoma.

abdominal organs posteriorly. A median sternotomy was then done and the right thoracic cage displaced laterally. The tumor was then delivered without great difficulty by rolling the whole mass laterally and dissecting the diaphragm from the constricted middle portion of the tumor. The tumor was found to arise from, and have its only firm attachment to, the seventh and eighth costal cartilages which were removed with it. After removal of the tumor the phrenic nerve was crushed, in its course along the pericardium, in order to facilitate the repair of the diaphragm. The diaphragm was repaired with interrupted silk mattress sutures and then sutured to the rectus sheath anteriorly. The divided sternum was brought together by kangaroo tendons which had been threaded through drill holes made in the two sides of the divided sternum. The remainder of the incision was closed with interrupted silk sutures.

Gross description: "The specimen consists of a huge tumor mass 30 cm. in its greatest diameter. It has an hour-glass constriction approximately in its midportion with the tumor extending on either side 18 cm. in one diameter and 12 cm. in the other. The surface is gray-white and nodular, being criss-crossed by depressed yellow-red trabeculae. The tumor has been opened in its long diameter revealing a central cavity containing gristly, gray-white tissue like that in the outer wall of the tumor and soft, yellow, friable tissue. Attached to the smaller (12 cm.) extent of the mass are two costal cartilages measuring 6.5 x 2.5 x 1.0 cm. These blend in with the cartilagenous tumor. Splitting of the tumor in halves by continuing the previous opening reveals no type of tissue grossly other than cartilage. The outer surface of the point of constriction is shaggy with dark red and gray tissue" (Fig. 6).

Microscopic Examination: "Numerous sections from various portions of the wall and center of the tumor reveal a typical cartilage proliferation in large islands with irregular zoning by hyaline, irregular bands. Scattered through this dedifferentiated cartilagenous tissue are numerous small areas of blue degeneration."

Pathological Diagnosis: "Chondrosarcoma."[14]

In 1947 the patient returned with evidence of recurrence of the tumor in the anterior chest wall. A second operation was done at which time a block dissection of the anterior chest wall including the anterior half of the sixth, seventh and eighth ribs were removed. Several small implants on the pericardium necessitated removal of a large portion of the left pericardium. Following this procedure, the patient made a good recovery and returned to work as a stenographer. On recent examination in February of 1950 recurrence again is present. However, this tumor has recurred slowly over a period of many years and has not metastasized. The patient is now over 70 years old.

Giant Cell Tumor

Giant cell tumors or osteoclastomas found in connection with the bony chest wall are exceedingly rare. Janes[10] reported 1 such case in 1939, Geschickter and Copeland[11] 1 case in 1949, while Buckles and Lawless[16] were able to collect eight cases from the entire literature. The physical and histologic characteristics of these cases followed those usually found in such tumors. Their origin is, as a rule, within the periosteum of the ribs or in their endosteal lining, and such tumors as they grow erode the cortex

but are kept constantly enclosed by the regenerating shell of periosteal bone. The central part of the mass becomes necrotic and softened by hemorrhage. In those with a slower growth tempo, a cyst-like structure may result with actual tumor tissue present only in the wall of such a cyst.[12] Microscopically such a tumor is made up of spindle-like cells, with large multinucleated "giant" epitheloid cells no different fundamentally from other foreign body giant cells. Usually such tumors grow slowly; they do not metastasize and recurrence does not occur after their complete removal.

Ewing's Tumor

As it involves chest wall structures, the so-called Ewing's tumor involves the clavicle more frequently than the ribs. The shafts are affected more commonly than the epiphyseal ends. Histologically this growth is a very vascular one composed of small round or ovoid undifferentiated cells without pleomorphism or giant cell formation. Multiplicity of lesions is common, especially in the late stages of the disease and metastases to lungs occur infrequently, but very frequently to lymph nodes. In this respect, Ewing's tumors differ from osteosarcomas. Roentgenologically it has the appearance of osteomyelitis with early bone formation and the spotty appearance of bone destruction. Diagnosis, however, depends largely on microscopic appearance. Clinically, this tumor is characterized by an immediate, sometimes dramatic, response to x-ray therapy, which, unfortunately, is always temporary with recurrency and death the rule. As a disease, it occurs primarily in the younger age group.

Myelomas

A myeloma is usually a systemic affection in which multiple growths spring simultaneously from the marrow of bones in various parts of the body. However, only a single bone, a rib or sternum, may be involved. In most instances other similar growths appear elsewhere in the body in the course of time, and the eventual prognosis is always poor. This type of tumor usually presents the x-ray appearance of a circumscribed rounded shadow of moderate density completely occupying and displacing the normal rib structure. When such a growth appears in the sternum, it may give the appearance roentgenologically of the case reported here. In this case, it is quite singular that multiple growths are now also occurring within the lungs. Were it not that plasma cells were so characteristically demonstrated, the original pathologic diagnosis might now be open to some doubt.

Case 4: Mr. M.K., 55 years old, was first seen by us on October 1, 1946. He gave a history of having had pain in the region of the sternum for four years. One year prior to this examination, the pain became so severe that he had to sleep in a sitting position. The month before his examination he noticed a swelling just to the left of the sternum at the level of the second intercostal space. Examination showed a definite mass about 3 inches in diameter just to the left of the sternum in the second intercostal space. No other abnormalities were found. Laboratory tests were not remarkable. The blood count was within normal limits as was also the urine. The sedimentation rate was 15 mm. in one hour (Westergren). X-ray examination of the chest showed a tumor of the anterior chest wall arising from the sternum (Fig. 7). There was also a small rounded area of increased density in the right lung field behind the right third rib. Operation was done through an anterior incision. The cartilage and part of the third rib were removed. The tumor was round, firm and encapsulated. It was adherent to the sternum and third costal cartilage and less densely adherent to the pericardium and great vessels at the hilus of the left lung. The tumor was removed together with part of the sternum. The patients postoperative course was uneventful. There has been no local recurrence after three years and seven months. However, there has been a slow progressive increase in the number and size of the areas of density in the lung fields which are presumed to be metastases. Microscopic sections of this tumor showed a typical plasma cell type of myeloma (Fig. 8').

Roentgenologic diagnosis is not always specific and a diagnosis of a single myeloma occurring within a rib is usually not made

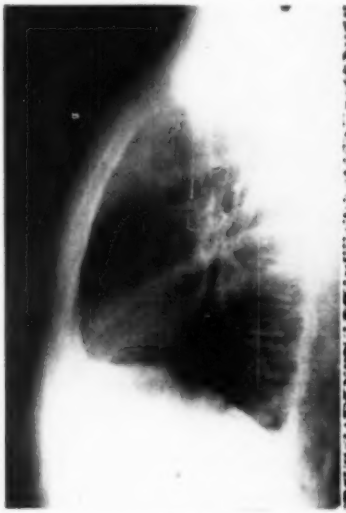

FIGURE 7

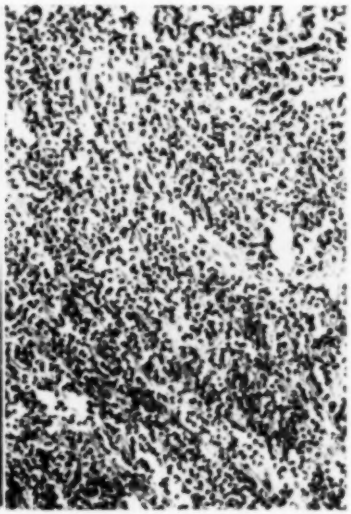

FIGURE 8

Figure 7: Lateral roentgenogram of plasma cell myeloma behind the sternum.
Figure 8: Photomicrograph of plasma cell myeloma.

preoperatively. However, should such a myeloma be expected, Bence Jones' proteinuria should be investigated, and further x-ray films of the bony structure taken. In the absence of confirmatory findings, suspicious tumors should be explored, for only by resection can an accurate diagnosis be made and other tumors more amenable to surgical treatment be discovered.

Tumors of Nervous Tissue

A very prominent group of tumors of the chest wall are those which originate in nervous tissue, either from the neurones themselves or from their supporting neuroglia. Innumerable designating names have been attached to this group, primarily depending upon their varying histologic structure and the interpretation of their origin. However, because they seemed to serve the purpose best, the names neurofibromas and neuroblastomas have come into common usage by the thoracic surgeon. Neurofibroma as implied here signifies a more or less slowly growing tumor, usually quite benign, located more frequently within the posterior mediastinum and posterior thoracic cage. In the latter case, its origin is usually from a thoracic peripherial nerve. Malignant tumors of this origin and location are usually referred to as the neuroblastomas with various qualifying terms such as neurofibrosarcoma, etc. In our experience malignant tumors of nervous origin have been found more frequently in children or young adults, are comparatively rapid growing and by the time of their discovery have already metastasized or infiltrated beyond the operative field. A third term, ganglioneuromas, is rather uncommonly used to describe tumors which arise retrocervically, retropleurally and retroperitoneally where they might have their origin within the sympathetic system. Such tumors contain chiefly non-medullated nerve fibers with imperfectly developed ganglion cells. When there is a predominance of the neuroglial elements, the qualifying term ganglioneuromas may be used. These tumors are usually considered as "benign," but nevertheless, instances of metastases have been reported.

Benign neurofibromas are by far the most common type of tumor originating in the nervous tissue. Harrington[13] was one of the first to recognize the frequency with which they confined themselves to the posterior thorax. This confinement is one of their distinguishing characteristics. Many lie directly upon the lateral surface of the vertebral column and consequently are described as mediastinal neurofibromas (Fig. 9). Others whose origin is more distal on a nerve trunk are probably best described as belonging to the chest wall group. Should their origin be from a spinal cord root, their growth may proceed, and often does,

through the intervertebral foramen and continue into the chest. Such tumors are aptly called "dumbbell types" with their small head growing intraspinally and giving rise to symptoms typical of cord tumors and with their larger distal segment enlarging intrathoracically and usually not producing symptoms. Their removal calls for the combined efforts of the neurosurgeon and thoracic surgeon. The most "anterior" tumor of this type which we have seen was a typical neurofibroma with a diameter of 3 cm. occurring in the course of the right seventh nerve in the posterior axillary line. However, by far the great majority are to be found within 2 to 3 cm. of the intravertebral foramen.

These benign neurofibromas result in only minimal symptoms, and at the present time the majority are discovered in the use of routine chest x-ray films. Because of their slow growth, adjacent structures are displaced gradually and have sufficient time to compensate for the displacement. We have recently encountered a tumor of this type which caused definite symptoms in an 86 year old woman whose left hemithorax was almost completely filled roentgenologically by a rounded, discrete, posteriorly placed tumor. Her symptoms were dyspnoea on exertion and inability to breathe while lying on the right side. This type of tumor is seldom

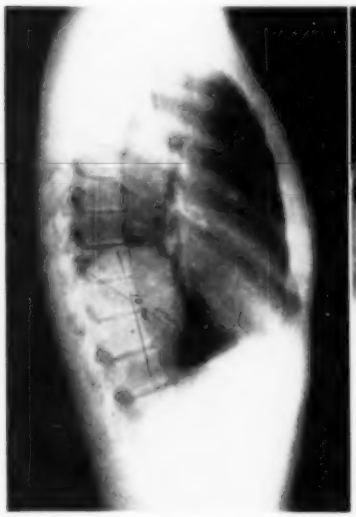

FIGURE 9

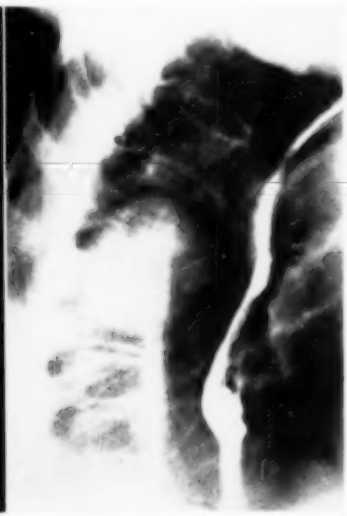

FIGURE 10

Figure 9: Lateral roentgenogram of chest showing typical location of neurofibroma.—*Figure 10:* Roentgenogram of bronchogenic cyst whose appearance is similar to neurofibroma. The esophagus contains barium.

associated with pain, and when it is, its supposed benignancy should be considered carefully.

Roentgenologically, these tumors are posteriorly placed, are of moderate hemogenous density, are rounded and quite discrete. The borders are smooth and regular in the majority of cases. Their size varies tremendously with their age. Because nothing but soft lung tissue and expansile thin pleura impedes their growth, they usually become remarkably round, although an occasional oblong type may be encountered. All are located retropleurally, and usually the pleura can be easily separated from the capsule of the tumor. Due to necrosis and liquifaction of their centrally located portions, some of these tumors may become partially cystic.

The preoperative diagnosis may be confused with that of posteriorly located bronchogenic cysts. In two instances we have made this mistake (Fig. 10). Posteriorly placed intrapulmonary lesions, such as "tuberculomas" or a "round" lesion of early malignancy may lead one into error. Cystic lesions of enteric origin, such as various reduplications of the gastrointestinal tract, may also confuse the diagnosis. Dermoid cysts situated in the extreme posterior mediastinum seem to be exceptionally rare. Pericardial cysts, also comparatively rare, are more anteriorly placed.

In spite of their benign symptomless nature and slow growth, the removal of neurofibromas should always be recommended, except under such extenuating circumstances as the advanced age of the 86 year old woman mentioned above. Although the diagnosis is relatively accurate, the term relative is not specific enough to protect the patient against an error in diagnosis. Open thoracotomy with thorough exploration and complete removal is the only recommended treatment. This procedure only rarely entails a wide excision of any chest wall structures unless the tumor proves to be malignant.

Treatment

The same concern, the same attitude, and the same philosophy should be used in approaching tumors of the chest wall as is the practice with tumors anywhere else in the body. The risk and desirable end results are no greater and no less than tumors situated within the abdomen. The use of the expectant attitude is as disasterous here as elsewhere. No tumor receives its definitive diagnosis except under the microscope, and the growth of no tumor can be said to have ceased unless it is completely separated from the body. These reasons alone are enough to demand exploration, if for nothing else than biopsy and a definite diagnosis, and complete removal whenever possible. Where the growth in-

volves the soft outer structures of the chest wall, wide excision is usually accomplished without too much difficulty and the resulting disability is usually not too great.

For complete eradication of some growths, sizeable segments of two or more ribs and their accompanying intercostal bundles must be sacrificed. This creates a large defect in the unyielding bony thorax. Complete stability of the chest wall should be the goal in the repair of such a defect. Paradoxical respiration with its diminution in pulmonary function and loss of forceful coughing will otherwise be the result. Janes'[10] method has already been mentioned but deserves repetition, for it is ingenuous in stabilizing the chest wall over a more or less large defect. In his method one or more adjacent ribs are separated from their sternal ends and are swung diagonally across the defect. Their divided ends and accompanying intercostal bundles are then anchored to another fixed structure of the chest wall.

The use of a tantalum plate has recently been quite successfully used by Beardsley.[15] Here a plate cut and moulded to cover the desired area is fixed in place by several sutures. Temporary stability is obtained. The plate, after formation of surrounding fibrous tissue and its subsequent contracture and thickening, can later be removed with the residual area being left in a fairly rigid condition. Attack upon the sternum has become a recognized procedure, particularly the manubrium. Excision of the manubrium was formerly thought to lead to great disability because of the resulting mobility of the medial clavicular ends. However, successful removal has been reported with only moderate resulting incapacity.[15]

RESUMEN

Se discuta la diagnosis y el tratamiento de tùmores del pared del pecho.

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Tumors of the Pleura

LOUIS L. FRIEDMAN, M.D., F.C.C.P.
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Tumors of the pleura may be primary or secondary. Primary tumors are exceedingly rare while secondary tumors are not uncommon. The most important and only primary malignancy of the pleura is the mesothelioma. In the 19th century the term, "tubercle-like lymphadenoma,"[6] was used to describe this tumor. Later the name, "endothelioma,"[7] was proposed for this malignancy because it was ascribed to a vascular origin. Recent reliable investigations together with the fact that the pleura is a mesodermal derivative have established the term mesothelioma as a more descriptive and appropriate identification of this tumor.

Epithelial and mesenchymal elements are both present in the pleura. The free surface is lined by a single layer of mesothelial cells which rest on a delicate elastic membrane. Beneath the membrane is found the loose connective tissue stroma. This is composed of collagenous and elastic fibers dispersed at various angles but generally parallel to the free surface of the pleura. Fibroblasts and macrophages constitute the predominant cellular elements. The subserous layer of tissue is responsible for the close adherence of the pleura to the related underlying structures. Tumors arising in the pleura will, consequently, display both epithelial and mesenchymal characteristics. Mesotheliomas are ordinarily composed of large epithelioid cells separated by collagenous fibers of tumor cell origin. The cellular elements have a tendency to arrange themselves as alveolar rests or rows. Unfortunately, not all pleural mesotheliomas present this typical histopathologic pattern. Pleomorphism and multidirectional lines of evolution complicate the proper identification and classification of this new growth. This tendency to frequent deviation has been paralleled by equally numerous attempts by well-intentioned investigators to prove the existence of more than one type of primary pleural malignancy. The problem of pleural malignancies, consequently, is clouded and confusing. Conclusive investigation and authoritative evaluation of this controversial problem have been limited by the paucity of cases available for study. Only one, and probably less than one, case in every one thousand postmortem examinations is a proved pleural mesothelioma.[6] If primary malignancies of the pleura do occur, the weight of the available evidence supports the contention that they are all mesotheliomas with inherent possibilities of wide structural variation.

This opinion, however, is not shared by all clinicians and pathologists.[5] There is a sizable group of reliable investigators who do not admit the possible existence of primary tumors of the pleura.[3,8] This contention is a very disarming possibility when one considers the large volume of literature which has been written on the subject of pleural mesotheliomas by innumerable, usually reliable investigators. It is true, nevertheless, that many pleural tumors diagnosed originally as mesotheliomas are proved eventually to be metastatic lesions from the underlying bronchopulmonary tissue or neighboring thoracic and even more distant organs.[6,8] A small primary malignant nodule in the lung is not infrequently the source of widespread pleural involvement. Unless the pulmonary tissue is examined diligently in all cases of suspected pleural mesothelioma, a small primary tumor nodule may be overlooked (Figs. 1 and 2). A high index of suspicion should be maintained at all times regarding this possibility in order to avoid erroneous diagnoses of pleural mesothelioma. Primary malignancies frequently arise in relation to the parietal pleura. They have their origin in the fascia of the intercostal muscles, nerve sheaths and other thoracic structures. Angiosarcomas, lipomyxosarcomas, neurosarcomas, round-cell or spindle-cell sarcomas, rhabdomyosarcomas or chondrosarcomas which arise from these tissues may be attributed erroneously to a pleural origin because of the intimate relationship of the parietal pleura to the structures of the thoracic wall. The known pleomorphic potentialities of pleural mesothe-

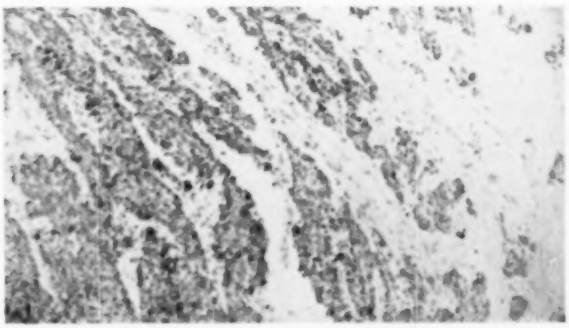

FIGURE 1: A diagnosis of pleural mesothelioma was considered in this instance based on the above histopathologic pattern observed in a section of tissue obtained from the region of the pleura. Recognizing the possibility of an erroneous conclusion, innumerable microscopic sections of the underlying bronchopulmonary tissue were examined. After diligent study, the lesion in the pleura was proved to be metastatic from a primary bronchogenic carcinoma. (Courtesy Dr. Joseph F. A. MacManus, Birmingham, Alabama).

liomas contribute to this pitfall in diagnosis. After careful consideration, this author is satisfied to concur in the opinion that such an entity as pleural mesothelioma does exist.[6,7] That it probably occurs much less frequently than one in every one thousand postmortem examinations also appears to be a valid assumption.

There are no primary benign tumors of the pleura. Just as the tumors which arise in relationship to the parietal pleura are malignant, those which occur in association with the visceral pleura are ordinarily benign. Fibromas, lipomas and chondromas have their origin in the subserous connective tissues. Giant sarcomas which arise in relation to the visceral pleura do not possess metastatic or invasive properties.[2] They grow slowly but may attain tremendous size. Primary tumors which arise in relation to the visceral pleura, with the possible exception of giant sarcomas, are asymptomatic. They are very small and usually discovered only by accident during surgical procedures or postmortem examinations. Surgical excision of these growths is the method of treatment.

Metastatic malignancies of the pleura are common. Any tumor which is capable of producing metastases may involve the pleura. Metastatic pleural lesions are most frequently secondary to the underlying bronchopulmonary tissue. Tumors of the breast also involve the pleura with great frequency. Malignant lesions of the esophagus are a frequent source of metastatic pleural involvement. Tumors of the other thoracic structures, stomach, adrenals, prostate, thyroid, pancreas and uterus are additional common sources of pleural metastases. Whenever a pleural malignancy is discovered it is imperative that these and other sites in the body be carefully scrutinized for a possible source of metastasis.

Primary, or metastatic malignant, lesions of the pleura may be

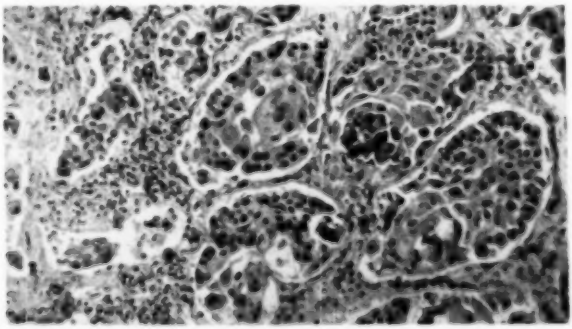

FIGURE 2: Microscopic section correctly identifying this tumor as a bronchogenic carcinoma.

diffuse or localized. Either variety produces hemorrhagic pleural effusions. Any unexplained pleural effusion, whether hemorrhagic or otherwise, however, in individuals past the age of 40, should arouse strong suspicions of a possible underlying malignant process. The chemical, physical and cytologic characteristics of the fluid depend upon the nature of the malignancy, duration, location and extent of pleural involvement. Occasionally the effusion develops the characteristics of a true hemothorax. The tendency to rapid reaccumulation following thoracentesis is a regular characteristic of effusions produced by malignant diseases of the pleura. Following the detection of hemorrhagic pleural effusion, indicated clinical and laboratory study to establish the correct etiology is in order. Since this discussion is concerned only with hemorrhagic effusions due to malignancies, those due to other causes are mentioned only for the sake of completeness. However, one should bear in mind that a hemorrhagic pleural effusion is not an uncommon manifestation of such clinical entities as pulmonary infarction, congestive heart failure, thrombocytopenic purpura hemorrhagica, cirrhosis of the liver, pneumonia, rheumatic fever, nephritis or pulmonary tuberculosis. Under certain conditions any pleural effusion may become hemorrhagic. Primary or metastatic malignancies of the pleura, however, are responsible for about 85 per cent of all hemorrhagic effusions. Although roentgenographic and fluoroscopic examinations of the chest are without rival in detecting pleural reactions, accurate identification of the etiologic factor depends upon other clinical and laboratory studies.

Diagnostic thoracentesis should be performed as soon as the presence of pleural effusion has been determined. An anticoagulant should be added to the aspirated material to avoid clotting. Complete withdrawal of the effusion should be attempted in order to facilitate more satisfactory roentgenographic examination of the underlying lung. There is a tendency among physicians to limit empirically the amount of fluid withdrawn during one thoracentesis. The author has practiced unlimited aspiration without any ill effects. Should the symptoms of dyspnea, cough, pulling sensation or pain in the chest develop during the procedure, the introduction of a small quantity of air usually suffices to control these manifestations of changing intrathoracic pressures and position of the heart and great vessels. Aspiration of the effusion may then be continued until all the fluid is withdrawn repeating small injections of air as necessary. The apprehensive patient may be calmed with suitable doses of a barbiturate or other sedative prior to thoracentesis. Production of pneumothorax in the presence of a hemorrhagic pleural effusion due to a malig-

nancy is actually desirable for diagnostic purposes. Introduction of air should be minimal or avoided after the diagnosis is established. Since bloody effusions are excellent culture media for bacteria, strict asepsis must be practiced in performing each thoracentesis. To avoid troublesome complications such as pyohemothorax, penicillin or any other suitable antibiotic agent should be instilled into the pleural cavity and along the needle tract when thoracentesis is completed.

A minimum of 5,000 to 6,000 red blood cells per cubic millimeter is required for the gross recognition of hemorrhagic effusions. The color of the fluid depends upon the number of red blood cells, their condition and length of confinement in the pleural cavity. Degeneration of the red corpuscles is followed by changes in the hemoglobin which may produce a brown or deep amber-colored effusion. Eosinophil cells may be present in unexplainably large numbers. Examination of the circulating blood in these instances may also reveal an absolute eosinophilia. When Hodgkin's disease is being considered, this finding may be misleading. The peripheral blood study is helpful ,however, in cases of leukemia involving the pleura. Determination of the specific gravity and chemical analysis of hemorrhagic pleural effusions due to a malignancy are of no diagnostic value. The fluid may be thin and easy to aspirate or very thick and gelatinous and difficult to remove. Cytologic examination of properly prepared specimens of the hemorrhagic fluid by a competent histopathologist is the most important diagnostic study. Frequently malignant cells will be detected in the aspirated material. Tumor identification usually follows. Unfortunately, even in the presence of a known malignancy, malignant cells cannot always be detected in the pleural fluid in spite of repeated diligent study.

If identification of the tumor does not follow pleural fluid examination, other diagnostic studies should be considered. A careful search for enlarged lymph nodes or overt tumor growths in the immediate thoracic or more distant regions of the body may be fruitful. The breast, thyroid, uterus and prostate deserve special attention. Surgical biopsy of an abnormal lymph node or other lesion may provide the diagnosis after histopathologic study. Aspiration biopsies of the pleura are generally failures. Punch biopsies with a Vim-Silverman needle are more successful in these instances. Larger and more satisfactory pieces of tissue are made available for study by this latter procedure. Many condemn the use of aspiration or punch biopsies because of the possible danger of stimulating or actually producing metastatic lesions. In the presence of malignant pleural effusions one need not hesitate to perform either an aspiration or punch biopsy of the pleura.

This observer has heard and read many reports of secondary seeding and metastasis following either of these procedures but has never experienced or witnessed these misfortunes. Furthermore, how much significant harm can one produce in the presence of either a primary or secondary pleural malignancy? Actually, and with rare exceptions, determination of an accurate diagnosis in these instances is of academic interest only.

Since malignant tumors of the pleura are frequently secondary to primary lesions of the bronchopulmonary tissue, bronchoscopic examination should be performed routinely. The responsible primary tumor may be visualized. Specimens of bronchopulmonary secretions and frequently biopsy material may be obtained in this fashion for histopathologic review. Additionally, careful study of the position and configuration of the bronchoscopically accessible portions of the tracheo-bronchial tree may be of valuable diagnostic assistance. Bronchography should be used for indirect visualization of those portions of the tracheobronchial network which are inaccessible for direct bronchoscopic study. Carefully conducted x-ray and fluoroscopic examination of the lungs in various positions are especially helpful. Examination of the gastrointestinal tract with an opaque material may reveal the source of pleural metastasis. A high serum acid phosphatase level will incriminate the prostate. Alkaline phosphatase determination is of no special value. If existence and identification of a malignancy is not established or confirmed by the enumerated procedures, one should not hesitate to recommend thoracoscopic examination of the pleura and, preferably, a diagnostic thoracotomy. Many other diagnostic procedures may be attempted. In this presentation, however, only those procedures which are most frequently indicated, practicable and generally useful have been discussed and evaluated.

Since mesothelioma is considered the only primary malignancy of the pleura, it deserves some special attention. Pleural mesotheliomas may occur in all ages, but are most frequent in the adult age group.[6] Males are affected twice as often as females.[1] Both hemithoraces are probably involved with equal frequency but opinion is divided on this point.[4,6] The onset of the tumor is insidious. Nonproductive cough and pain in the chest are early symptoms. Fever becomes a manifestation when secondary infection supervenes but may occur without this complication. Later, the cough may acquire expectorant qualities. Massive accumulation of a hemorrhagic pleural effusion occurs with distressing regularity. Dyspnea ensues and quickly assumes the position of paramount concern among all other symptoms. The patient becomes cachetic with startling rapidity. Loss of weight, anemia

and weakness are typical observations. Dependent edema may occur at any stage of the illness. The panorama of symptoms changes frequently to correspond with the rapid growth of the tumor. Frequent thoracenteses are indicated for the palliative relief of dyspnea. Resistance to the introduction of the aspirating needle is usually very marked. As previously indicated, the benefits of thoracenteses are very temporary since the fluid re-accumulates rapidly. Occasionally daily thoracenteses are necessary to relieve the subsequent cardiorespiratory embarrassment. The fluid is easily aspirated early in the illness but gradually it becomes thicker and more difficult to remove. Re-accumulation has been observed to occur less rapidly after the pleural fluid assumes a thicker character. There is no effective treatment for pleural mesothelioma, or any other malignant involvement of the pleura. Metastases are common and the tumor may extend to involve the other pleural cavity, pericardium, peritoneum and capsules of abdominal viscera. Patients usually die within six to twelve months following detection of the tumor.

SUMMARY

1) The controversial subject of pleural tumors has been reviewed.

2) Although very rare, mesotheliomas are probably the only primary pleural tumors.

3) Malignant tumors of the pleura are predominantly metastatic or due to tissue continuity.

4) Clinical and laboratory aids most useful for accurate identification and evaluation of malignant growths of the pleura have been enumerated and discussed.

RESUMEN

1) Se revisa el asunto de la controversia de los tumores de la pleura.

2) Aunque muy raros, probablemente los mesoteliomas son los únicos tumores primarios de la pleura.

3) Los tumores malignos de la pleura son predominantemente metastáticos o debidos a continuidad tisular.

4) Se enumeran y se discuten los procedimientos de laboratorio y los clínicos que son útiles auxiliares para la identificación exacta de las neoplasias malignas de la pleura.

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Editorials

Doctors are noted for their ability to disagree about many things. There is often wide divergence of opinion as to the surest, safest and most expeditious way to help the sick. For example, sit in on a weekly conference in any tuberculosis sanatorium while, let us say, a moderately advanced case is up for decision. One staff physician wants to continue bed rest alone, another pneumothorax, another pneumoperitoneum, and another, phrenic interruption or thoracoplasty. Then these methods with or without streptomycin or PAS, alone or together, are suggested. It would take a mathematician with a slide rule to calculate the total number of combinations.

With tuberculosis we have a disease about which the cause is known, yet there is an admitted wide divergency of opinion as to therapy. The opposite situation exists in regard to tumors. In spite of the fact that the etiology is unknown, doctors agree that surgical excision is our best weapon. In this issue all lesions described by the various authors, with the exception of metastatic growths and lymphomas, present problems best solved by removal.

Although we may have decided to agree as to the best weapon available today for tumors, there still is apparently much room for argument. In the search for early intrathoracic disease the x-ray is our best trouble indicator, but we see shadows, not the actual object. Here is where the disagreement and the delay begin. Each doctor has his own interpretation of what caused the shadow.

Unfortunately, the less urgent abnormal shadows usually receive the most expeditious handling. Benign tumors cast a more discrete shadow and one of greater contrast than malignant ones. In the past, patients with abnormal shadows due to benign tumors, whether symptoms were present or not, have usually been advised to be operated upon immediately. The "shadow that should not be there" is so obvious that the untrained eye of the patient, when shown the film, sees trouble in the future and accepts the good advice of his doctor.

Cancer, the most urgent of all shadow-producing lesions, is not as obliging as the benign tumor. If a cancer is situated in the periphery of the lung, its shadow may for a long time look exactly like a tuberculoma. If the cancer occludes a segmental bronchus, the atelectatic segment and superimposed aerated parenchyma on either side will produce a shadow which simulates a tuberculous infiltrate when in the upper lobe or virus pneumonia if it is in the lower lobe.

Chest specialists, confronted with the responsibility of accurately

sorting out shadow-producing lesions must gear up investigative procedure to meet the demands of the cancer potential. In tuberculosis case-survey work the factor of time is not of such crucial importance. However, loss of time in cancer recognition may rob the patient of his one and only chance to live.

It is fortunate that it has been possible to assemble within this one volume so many valuable papers on the subject of thoracic tumors. So much of our time is spent looking at shadows it is well to be reminded again and again that each shadow is produced by an object which may have the power to destroy the individual and that you and I can do something about it.

Richard H. Overholt, M.D., F.C.C.P.

PARABLE FROM PULMONIA

Once upon a time in the land of Pulmonia, a new king was crowned. As a prince, he had led a most sheltered life, and upon his ascendency he was distressed to learn of the evil Dragon existent within the Kingdom which killed, each day, one hundred of the citizens. He called his Grand Vizier unto him.

"Tell me of this Dragon," he demanded.

"Ours is but one of many, Sire," said the Vizier. "Every country has its own Monster. These differ in certain particulars such as speed of attack and number of citizens consumed per diem. Some are cowardly and molest only women. Others attack only men. Our own Colossus is gentlemanly in that it takes many more men than women. All of the Dragons have two things in common. They are vulnerable only from the anterior approach, and they breathe a fiery breath for a distance of twelve paces."

"The Dragon must be killed!" shouted the young King.

"Those were the first words your Royal Father spake when he was crowned," said the Vizier, "and at that time our Dragon was killing only fifty citizens per diem. Be assured that steps are being taken. The International Society of Grand Viziers conducts an annual Congress at which information is exchanged, data are accumulated, progress plans are written, and money is collected to serve those alchemists working on the project. We are in complete agreement on certain things, the most important of which is the devising of a great Spear, fifteen paces in length, of an alloy steel so light as to be maneuverable, so well-tempered as to withstand the fiery breath, and so sharp as to penetrate the monstrous vitals. We are not as yet of unanimous opinion, I am sorry to say, concerning the magical incantations and the mystic inscriptions which must fulfill the destiny of the Spear."

"I can see," interjected the King, "that with such a Spear the Dragons can be killed. But meanwhile, what of the innocent people?"

"We have not neglected that phase, Sire," responded the Vizier, "by international law we have established the finest protective measures. In each country lookout stations are established at the most strategic points. Should the Dragon attack within the perception of these sentinels, a great bell is rung. This activates trained warriors, mounted on the fastest steeds, and armed with the sharpest swords. Since Dragons are prone to play an insidious game of cat-and-mouse before consuming the victim, often the warriors arrive before the kill, and by hacking at the Titan's tail, so divert it that its quarry may be rescued. Still another protective measure that we have internationally decreed is regularly to send out heralds proclaiming to the people the habits and methods of Dragons, so that the citizens may know of any approach and run to the protection of the warriors with the sharp swords."

The King nodded approval. "This is all intelligent work, and well done." Then he frowned, thoughtfully. "There is still one thing that disturbs me. You stated that, at my father's coronation, the Dragon killed fifty citizens each day, but I know that now the daily toll is one hundred. Is this increase international?"

"No, Sire," answered the Vizier, "this tragic increase is peculiar to our own country. There are several interesting theories on this subject. The Vizier from Gastropia, an arrogant man since his Dragon is the most omnivorous, advances an interesting hypothesis. The other countries have high mountains and deep valleys. Wind, when present, is gusty and foul. An obscurative miasma is cast over these lands, thus offering equal opportunities for ambush and refuge. Our country has flat open country and a constant wind which sweeps away all vapors. He contends that the Dragon has taken better advantage of the increased visibility than have we. My own theory is that in recent years certain gases have entered into our atmosphere. Because of the steady winds peculiar to our country, these fumes have been more available to our own Colossus, and they have given him a stimulation."

The King mused and pondered. Then he spoke with the wisdom of his royal lineage. "Hypotheses may be right or wrong. One fact I know. The clear air of our kingdom, devoid of fogs, obscured only by a few fluffy clouds, can be our greatest protection against the Monster. Let there be built more watchtowers, as numerous and as high as the Royal purse can afford. Let the citizenry be tested to find those possessing eyes with the sharpness of the soaring eagle, and induce them to become our sentinels. Encourage the greatest cooperation between the lookouts, the people, and

our warriors. Until your magic Spear has slain this Dragon, we can best save the people by seeing our enemy."

Archives of Atwell.

Closing Comment

The Spear of prophylaxis against cancer no longer seems an improbability, but until it is finally forged and in common use, we must continue to extend the weapons at our hand. The scalpel, the microscope, and the roentgen-ray, presented and coordinated by knowledge, can find greater use through man's ingenuity.

Diagnostic radiology, younger than surgery and pathology, is our most potent weapon in the search for curable cancer of the lung. In its present form it is being extended to become of increasing value. For its future form it can find a lesson in the development of histo-pathology,—the constant improvement of methods for better presentation of more minute detail. Radiology's fulfillment must follow this same concept. The ability to study by magnification the image of living tissue *in situ* can be a great step forward in research and early diagnosis.

Richard H. Overholt, M.D., F.C.C.P.

COMMENT

Tumors of the chest now constitute a sizable segment of the physician's practice in diseases of the chest. Not long ago, many persons had these conditions diagnosed as tuberculosis and were sent to sanatoriums where their deaths were credited to this disease except for the few on whom necropsies were performed. An increasing awareness of the frequency with which tumors appear in the chest, together with more recently acquired diagnostic aids, has greatly stimulated the consideration of and search for tumors whenever there is evidence of disease in the chest that cannot be promptly diagnosed. Many tumors when diagnosed promptly can be treated successfully, primarily by surgery. In this issue of *Diseases of the Chest*, Dr. Andrew L. Banyai has again demonstrated his superior ability and judgment in selecting titles of practical value. He has further shown these fine qualities in his choice of authors with reference to experience and accomplishment in both the diagnosis and the treatment of tumors of the chest. In addition, Dr. Banyai has devoted a large amount of time to editing this special issue, for all of which he is deserving of high praise. It is an unusual pleasure to speed on its way this issue with its fine array of articles to physicians in diseases of the chest throughout the world.

J. Arthur Myers, M.D., F.C.C.P.

PAUL AKERS TURNER, M.D., F.C.C.P.

PAUL AKERS TURNER, M.D., F.C.C.P.

1882 - 1950

To visit the home of Paul and Alice Turner was to experience Southern hospitality at its best. In this home culture was in evidence everywhere and the highest ideals of human endeavor were always manifested. No guest could leave their home without being inspired to do better in all of life's worthwhile activities. Paul Turner was born in Portland, Maine, on September 11, 1882. He received the Bachelor of Arts degree from Amherst College in 1904, and five years later, the degree of Doctor of Medicine from Columbia University College of Physicians and Surgeons. He then completed an internship at Bellevue Hospital, New York. In 1910 he began the practice of medicine in Seattle, Washington, and served as medical superintendent of the Seattle City Hospital from 1911 to 1917.

Nineteen hundred and seventeen was a notable year in his life, for it was then that he married Alice Hayden, who, for the next third of a century, was helpful in assuring the success of his professional life. They reared two daughters, Barbara and Joeann, who contributed greatly to the happiness and pride of their parents. After serving as director of health of the State of Washington from 1921 to 1925, Paul was appointed to the superintendency and medical directorship of Hazelwood, Kentucky State Tuberculosis Sanatorium. There, for the next quarter of a century he devoted his professional life to the thousands of patients who entered this institution. There was nothing that Paul Turner would not do to encourage and help the tuberculous. He was quiet and unassuming, had a good sense of humor, a twinkle in his eye and a smile for everyone. He was a physician of unusual skill, was sincere, honest, truthful, sympathetic, and devoted to his work and his patients, who affectionately called him "Pop." At the same time, he maintained excellent discipline to the benefit of the patients, and whenever the occasion arose he could express himself in no uncertain terms. All of these qualities made him an excellent sanatorium director.

Dr. Turner always kept abreast of the times and brought to his institution the most modern methods of diagnosis, treatment and prevention. He introduced all stages of collapse therapy, including the most recent major operative procedures such as segmental resection, lobectomy and pneumonectomy. It has been said that more modern thoracic surgery was being employed in the Kentucky State Sanatorium than in any other institution of its size. He procured antibiotics and other new drugs as soon as their value had been proved and they could be made available to him.

Dr. Turner was a valuable participant in medical organizations. He was secretary of the Southern Sanatorium Association from 1935 to 1937; president of Southern Tuberculosis Conference in 1939, and of the Kentucky State Hospital Association, 1940. He held membership in the American Medical Association, National Tuberculosis Association, American Trudeau Society, American Hospital Association and Southern Medical Association. His keenest interest was in the American College of Chest Physicians, of which he was a founder. Throughout the years he gave unstintingly of his energy and talent. He was elected second vice-president of the Southern Chapter in 1944, first vice-president in 1945 and president in 1947. Because of his outstanding work and the admiration which physicians had for him, he was elected first president of the Ken-

tucky Chapter of the American College of Chest Physicians on October 5, 1949. For many years he was regent of the American College of Chest Physicians and in 1949 was elected chairman of the Board of Regents. He conducted the meetings of the Board in a most dignified and fair manner. His published papers were on such subjects as *Public Health Problems of the Pacific Coast*, 1922; *Benign Tumors of the Bronchus*, 1934; *Early Diagnosis of Pulmonary Tuberculosis*, 1935; *Extrapleural Pneumonolysis*, 1935. One of his most outstanding papers, *Humanity in the Practice of Medicine, with Especial Reference to the Tuberculous*, was presented at the meeting of the Southern Chapter of the American College of Chest Physicians at Baltimore, Maryland, November 24, 1947.

Dr. Turner volunteered for service in World War I and was overseas as surgeon with the rank of first lieutenant with the 163rd field hospital. He was also with the occupational army in Germany and at the conclusion of the war was promoted to captain.

Wherever he went, Dr. Turner immediately became popular. At Amherst College he was a member of the Phi Delta Theta fraternity and at Columbia, Nu Sigma Nu medical fraternity. When the Amherst class of 1904 held a reunion in 1949, he was elected president of the class for a period of five years. He was a member of the Kiwanis Club and for a period of six years had perfect attendance. He held membership in the Riverside Boat Club and the Coast Guard Flotilla. His main recreations consisted of boating, fishing, photography and gardening.

Paul Turner was enjoying his usual good health. The opening of a part of the new State Sanatorium was to occur April 14. After finishing the day's work on April 13, he left the office and went to his home, where he suddenly died at 4:30 P. M. In a brief time messages began to reach the home from almost everywhere. They came from persons in all walks of life, including many former patients, the Governor of Kentucky, the State Commissioner of Finance, professional workers, including large numbers of physicians, many of whom he himself had trained in the field of diseases of the chest. All messages contained an expression of admiration and the high esteem in which Paul was held. A large number of persons from Kentucky and other states assembled before his remains were buried in the Bluegrass of the Resthaven Cemetery at Louisville.

A bronze plaque is to be placed on his surgery door with the inscription, "In Memory of Dr. Paul A. Turner — Hazelwood Sanatorium, 1925-April 13, 1950 — No greater love hath any man than he who lay down his life for others."

Many persons are living today who would have long since died had it not been for Dr. Turner's treatment. Large numbers of others are living who never knew him because of the treatment administered by the physicians whom he taught. His contributions to medical literature, the information that he transmitted to students, as well as physicians in practice in such a wide area, will insure the perpetuation of the activities which he promoted, and thus he will continue to participate in the endeavors against diseases of the chest as carried on by physicians everywhere.

Sixteenth Annual Meeting of the College

The twenty-second of this month marks the opening day of the Sixteenth Annual Meeting of the College. San Francisco is host to our meeting this year and the St. Francis Hotel will be College headquarters. The administrative meetings and conferences of the College will be held on Thursday, June 22 and the scientific sessions will begin on Friday morning the 23rd.

A splendid program of scientific material covering all phases of diseases of the chest has been arranged by program chairman Dr. H. J. Moersch of the Mayo Clinic, Rochester, Minnesota. Those who have assisted Dr. Moersch in arranging the program are Drs. Osler A. Abbott, Atlanta, Georgia, Paul H. Holinger, Chicago, Illinois, Edwin R. Levine, Chicago, Illinois, Karl H. Pfuetze, Cannon Falls, Minnesota, Leo G. Rigler, Minneapolis, Minnesota, and R. H. Sundberg, San Diego, California.

Releases concerning the meeting have been mailed to all members and from information received at the Executive Offices it is anticipated that there will be a good attendance. The Section on Diseases of the Chest of the American Medical Association will have an excellent program on Wednesday, June 28 and Thursday, June 29, and outstanding exhibits on diseases of the chest will be shown all week in the Section on Scientific Exhibits of the American Medical Association.

All members of the College should make it a point to register for the Section on Diseases of the Chest in the American Medical Association.

College Chapter News

ARIZONA CHAPTER

At the annual meeting of the Arizona Chapter, held on May 1st in Phoenix, the following officers were elected:

John W. Stacey, M.D., Tucson, President
John L. Cogland, M.D., Phoenix, Vice-President
Leslie B. Smith, M.D., Phoenix, Secretary-Treasurer.

NEW ENGLAND STATES CHAPTER

The following officers were re-elected at the annual meeting of the New England States Chapter held in Boston on May 10th:

Moses J. Stone, M.D., Boston, Massachusetts, President
Hugh Boyle, M.D., New Bedford, Massachusetts, Vice-President
John B. Andosca, M.D., Cambridge, Mass., Secretary-Treasurer.

PACIFIC NORTHWEST CHAPTER

Officers elected at the annual meeting last fall of the Pacific Northwest Chapter of the College are as follows:

Frederick Slyfield, M.D., Seattle, Washington, President
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THIRD ANNUAL POSTGRADUATE COURSE
IN DISEASES OF THE CHEST
AMERICAN COLLEGE OF CHEST PHYSICIANS
APRIL 10 - 14, 1950
WARWICK HOTEL
PHILADELPHIA, PA.

Third Annual Postgraduate Course Held in Philadelphia

The Third Annual Postgraduate Course in Diseases of the Chest sponsored by the Pennsylvania Chapter of the College and the Laennec Society of Philadelphia was presented at the Warwick Hotel, Philadelphia, during the week of April 10-14, 1950. Dr. Chevalier L. Jackson served as Chairman of the course, Dr. Leon H. Collins Jr., as Vice-Chairman and Drs. Katharine R. Boucot, Louis Cohen, Robert V. Cohen, David A. Cooper, Burgess Gordon, William A. Lell, Esmond R. Long and Martin J. Sokoloff as members of the postgraduate course committee. Dr. J. Winthrop Peabody, Chairman of the Council on Postgraduate Medical Education of the College, and Dr. Edward Lebovitz, President of the Pennsylvania Chapter, served as ex-officio members of the committee.

Forty-eight physicians registered for the course representing 14 states and Canada. A photograph of the group appears on the opposite page. A banquet was held on Tuesday evening, April 11, at the Warwick Hotel which was attended by seventy-five instructors, attending physicians and guests. Dr. W. W. Peter, Chief of the Medical Section of the Institute of Inter-American Affairs, Washington, D. C., was the guest speaker.

The following physicians were registered for the course: Irene V. Allen, East St. John, N. B., Canada; R. M. Anderson, Hackensack, New Jersey; Aubrey L. Bradford, Ft. Bragg, North Carolina; E. C. Brunner, Miami, Florida; Arthur J. Carbonell, Ft. Belvoir, Virginia; Louis Cherniack, Winnipeg, Canada; James A. Crilly, Perry Point, Maryland; James G. Dickensheels, Pennsauken, New Jersey; Robert W. DuPriest, Phoenixville, Pennsylvania; B. J. Ellmers, New Milford, New Jersey; Donald J. Francis, Camp Lee, Virginia; Elmer W. Fugitt, Ft. Dix, New Jersey; T. G. Heaton, Toronto, Canada; Elmer F. Herring, San Fernando, California; C. W. Hickam, Pulaski, Virginia; Robert K. Irvine, Coatesville, Pennsylvania; T. S. Jennings, Martinsburg, West Virginia; Herman B. Kaufman, Zanesville, Ohio; David Kaung, Cleveland, Ohio; Emmett L. Kehoe, Washington, D. C.; Gordon F. Kincade, Vancouver, B. C., Canada; Israel E. Kirsh, Oak Park, Illinois; Phillip T. Knies, Columbus, Ohio; Joseph S. Koehler, Dayton, Ohio; Samuel Lobe, Cleveland, Ohio; L. Macpherson, East St. John, N. B., Canada; A. C. McKenna, Hamilton, Canada; George M. Miller, Rahway, New Jersey; Virgil F. Neumann, New London, Connecticut; Katherine Pardee, Wallum Lake, Rhode Island; William B. Patterson, Huntingdon, Pennsylvania; Max N. Pusin, Jersey City, New Jersey; John W. Raulston, Ft. Monmouth, New Jersey; Edward S. Ray, Richmond, Virginia; P. M. Ross, Canton, Ohio; W. E. Roye, Richmond, Virginia; Hyman Rubinsky, Washington, D. C.; Edward W. Schoenheit, Asheville, North Carolina; William J. Seiferth, Aspinwall, Pennsylvania; Warren B. Shepard, Pittsburgh, Pennsylvania; John A. Sims, Alexandria, Virginia; Irvin Sussman, Bridgeton, New Jersey; Gerald M. Tierney, Ft. Meade, Maryland; William B. Townsend, Columbia, South Carolina; Donald W. Tripodi, Providence, Rhode Island; John R. Troxell, Winchester, Virginia; Walter B. Watson, Phoenixville, Pennsylvania; Ruth W. Wilson, Beaver, Pennsylvania.

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Two full time staff physicians with at least one year's training and experience in tuberculosis wanted for 250 bed tuberculosis hospital in Ohio. Salary from $5,500 to $6,500 per year plus full maintenance for doctor and family. Active medical and surgical service, broad program of case finding and tuberculosis program being organized. Please address Box 212A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

There are several vacancies for resident physicians on Medicine at Triboro Hospital, effective July 1, 1950. Triboro Hospital is a municipal tuberculosis institution with 625 beds. The educational opportunities are excellent and there is a good training program. The residency is approved and for those who wish to qualify for their boards in internal medicine, credit is given for one year's training at Triboro. The salary is $1,560 per year and single maintenance. Those interested please write or phone the Medical Superintendent, Triboro Hospital, Jamaica 2, L. I., New York.

Staff physician for 105 bed private tuberculosis sanatorium in central Pennsylvania. Medical and surgical phases covered, including bronchoscopy, out-patient service. Excellent opportunity to learn. Pennsylvania license or reciprocity required. House and maintenance for physician and family, congenial surroundings. Inquire medical director or superintendent, Devitt's Camp, Allenwood, Pennsylvania.

Positions open for physicians in large tuberculosis hospital. Salaries from $4,800 to $7,320 annually. Must be eligible for license to practice in Georgia. Contact Personnel Office, Battey State Hospital, Rome, Georgia.

Assistant Medical Director wanted for Nebraska Hospital for Tuberculous; 200-bed hospital offering all phases of treatment of tuberculosis. Knowledge of tuberculosis preferred. Must be eligible for Nebraska license. Living quarters and maintenance furnished. Salary approximately $5,000 yearly. Inquire Medical Director, Nebraska Hospital for Tuberculous, Kearney, Nebraska.

Residency in division of medicine, chest service, university hospital. Duties include work in field of various chest diseases. One year beginning July 1, $25.00 per month salary. Credit toward American Board of Internal Medicine. Please address Box 212A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

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DISEASES OF THE CHEST

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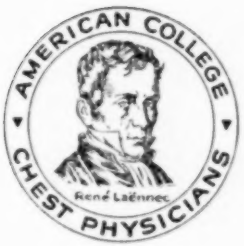

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JANUARY - JUNE, 1950

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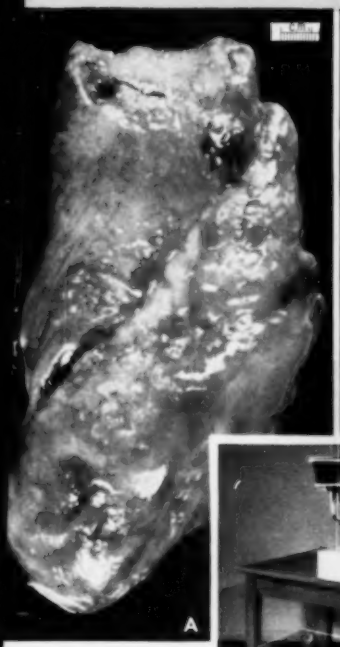
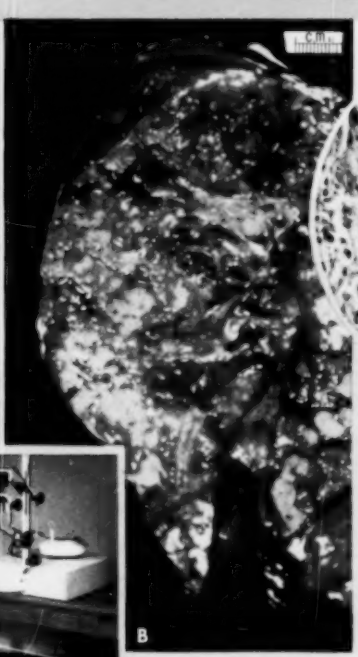
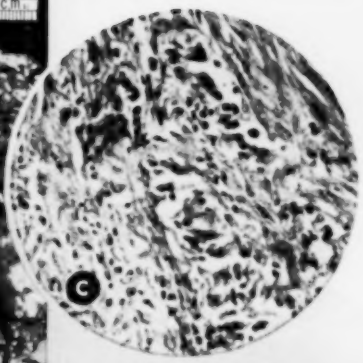
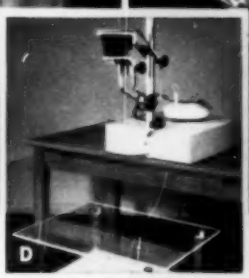
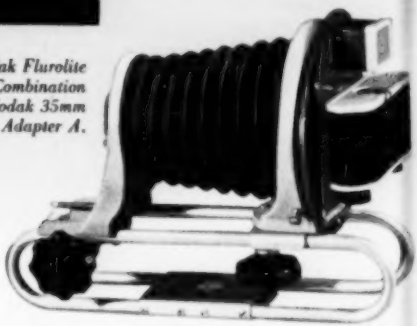






Reproductions **A** *and* **B** *show gross aspects of diseased lung after pneumonectomy. Reproduction* **C** *shows photomicrograph made from histological section of affected lung. Figure* **D** *shows setup of Kodak Flurolite Enlarger fitted with Camera components for the photography of gross specimens.*





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